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Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:SSPTANXR1625

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS  3  MAR 16  CASREACT coverage extended
 NEWS  4  MAR 20  MARPAT now updated daily
 NEWS  5  MAR 22  LWPI reloaded
 NEWS  6  MAR 30  RDISCLOSURE reloaded with enhancements
 NEWS  7  APR 02  JICST-EPLUS removed from database clusters and STN
 NEWS  8  APR 30  GENBANK reloaded and enhanced with Genome Project ID field
 NEWS  9  APR 30  CHEMCATS enhanced with 1.2 million new records
 NEWS 10  APR 30  CA/CAplus enhanced with 1870-1889 U.S. patent records
 NEWS 11  APR 30  INPADOC replaced by INPADOCDB on STN
 NEWS 12  MAY 01  New CAS web site launched
 NEWS 13  MAY 08  CA/CAplus Indian patent publication number format defined
 NEWS 14  MAY 14  RDISCLOSURE on STN Easy enhanced with new search and display
                  fields
 NEWS 15  MAY 21  BIOSIS reloaded and enhanced with archival data
 NEWS 16  MAY 21  TOXCENTER enhanced with BIOSIS reload
 NEWS 17  MAY 21  CA/CAplus enhanced with additional kind codes for German
                  patents
 NEWS 18  MAY 22  CA/CAplus enhanced with IPC reclassification in Japanese
                  patents
 NEWS 19  JUN 27  CA/CAplus enhanced with pre-1967 CAS Registry Numbers
 NEWS 20  JUN 29  STN Viewer now available
 NEWS 21  JUN 29  STN Express, Version 8.2, now available
 NEWS 22  JUL 02  LEMBASE coverage updated
 NEWS 23  JUL 02  LMEDLINE coverage updated
 NEWS 24  JUL 02  SCISEARCH enhanced with complete author names
 NEWS 25  JUL 02  CHEMCATS accession numbers revised
 NEWS 26  JUL 02  CA/CAplus enhanced with utility model patents from China
 NEWS 27  JUL 16  CAplus enhanced with French and German abstracts
 NEWS 28  JUL 18  CA/CAplus patent coverage enhanced

 NEWS EXPRESS  29 JUNE 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  of commercial gateways or other similar uses is prohibited and may
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result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:26:24 ON 20 JUL 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 12:26:32 ON 20 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 19 JUL 2007 HIGHEST RN 942942-65-6
DICTIONARY FILE UPDATES: 19 JUL 2007 HIGHEST RN 942942-65-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

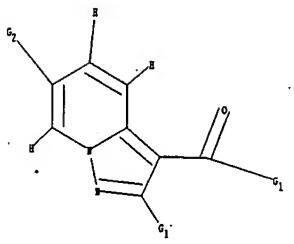
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

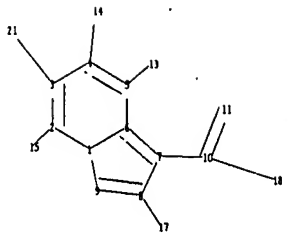
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10537313.str





chain nodes :
10 11 13 14 15 17 18 21
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
2-15 3-21 4-14 5-13 7-10 8-17 10-11 10-18
ring bonds :
1-2 1-6 1-9 2-3 3-4 4-5 5-6 6-7 7-8 8-9
exact/norm bonds :
1-2 1-6 1-9 2-3 3-4 3-21 4-5 5-6 8-9 8-17 10-11 10-18
exact bonds :
2-15 4-14 5-13 6-7 7-8 7-10
isolated ring systems :
containing 1 :

G1:H,Ak

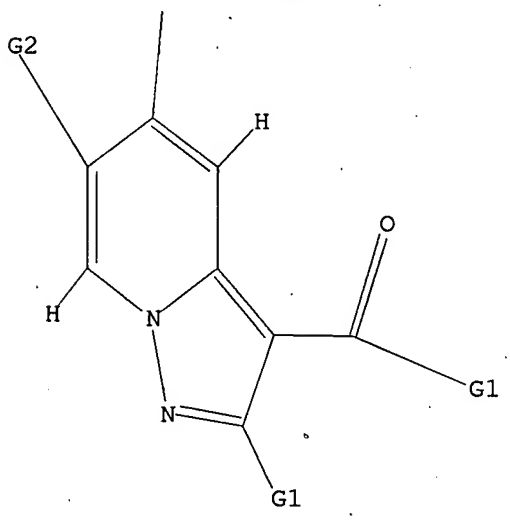
G2:H,O,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 13:CLASS 14:CLASS 15:CLASS 17:CLASS 18:CLASS 21:CLASS

L1 STRUCTURE UPLOADED

=> dl1
DL1 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 H,Ak
G2 H,O,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 12:26:55 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 223 TO ITERATE

100.0% PROCESSED 223 ITERATIONS 7 ANSWERS
SEARCH TIME: 00.00.01

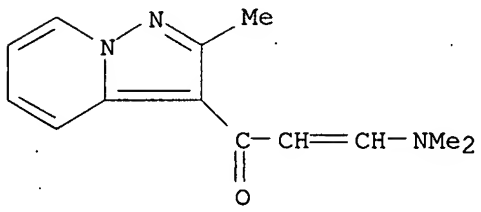
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 3565 TO 5355
PROJECTED ANSWERS: 7 TO 298

L2 7 SEA SSS SAM L1

=> d 1-7

L2 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2007 ACS on STN

RN 328064-17-1 REGISTRY
ED Entered STN: 20 Mar 2001
CN 2-Propen-1-one, 3-(dimethylamino)-1-(2-methylpyrazolo[1,5-a]pyridin-3-yl)-
(9CI) (CA INDEX NAME)
MF C13 H15 N3 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL



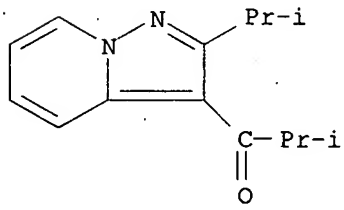
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2007 ACS on STN
RN 257626-03-2 REGISTRY
ED Entered STN: 01 Mar 2000
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-,
mononitrate (9CI) (CA INDEX NAME)
MF C14 H18 N2 O . H N O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

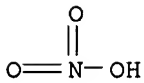
CM 1

CRN 50847-11-5
CMF C14 H18 N2 O



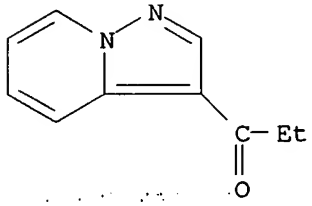
CM 2

CRN 7697-37-2
CMF H N O3



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

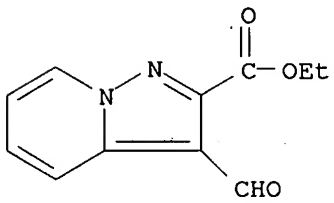
L2 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2007 ACS on STN
RN 151831-24-2 REGISTRY
ED Entered STN: 17 Dec 1993
CN 1-Propanone, 1-pyrazolo[1,5-a]pyridin-3-yl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pyrazolo[1,5-a]pyridine, 1-propanone deriv.
MF C10 H10 N2 O
SR CA
LC STN Files: CA, CAPLUS, CHEMINFORMRX



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

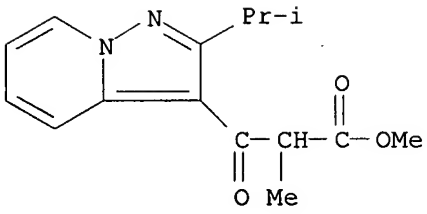
L2 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2007 ACS on STN
RN 151831-22-0 REGISTRY
ED Entered STN: 17 Dec 1993
CN Pyrazolo[1,5-a]pyridine-2-carboxylic acid, 3-formyl-, ethyl ester (9CI) (CA INDEX NAME)
MF C11 H10 N2 O3
SR CA
LC STN Files: CA, CAPLUS, CHEMINFORMRX



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

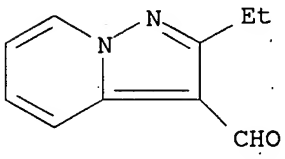
L2 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2007 ACS on STN
RN 141418-12-4 REGISTRY
ED Entered STN: 22 May 1992
CN Pyrazolo[1,5-a]pyridine-3-propanoic acid, α-methyl-2-(1-methylethyl)-β-oxo-, methyl ester (9CI) (CA INDEX NAME)
MF C15 H18 N2 O3
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

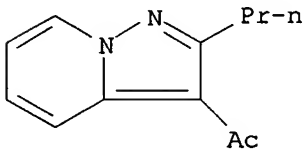
L2 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2007 ACS on STN
RN 73957-65-0 REGISTRY
ED Entered STN: 16 Nov 1984
CN Pyrazolo[1,5-a]pyridine-3-carboxaldehyde, 2-ethyl- (9CI) (CA INDEX NAME)
MF C10 H10 N2 O
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2007 ACS on STN
RN 59975-56-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Ethanone, 1-(2-propylpyrazolo[1,5-a]pyridin-3-yl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pyrazolo[1,5-a]pyridine, ethanone deriv.
MF C12 H14 N2 O
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s l1 full

```
FULL SEARCH INITIATED 12:27:39 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     4281 TO ITERATE

100.0% PROCESSED     4281 ITERATIONS                          103 ANSWERS
SEARCH TIME: 00.00.01

L3          103 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                             186.20     186.41

FILE 'CAPLUS' ENTERED AT 12:27:45 ON 20 JUL 2007
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 20 Jul 2007  VOL 147 ISS 5
FILE LAST UPDATED: 19 Jul 2007  (20070719/ED)

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They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3 full
L4          222 L3

=> s l4 and py<2002
      21897560 PY<2002
L5          158 L4 AND PY<2002

=> dibib abs hitstr 1-10
DIBIB IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d ibib abs hitstr 1-10

L5   ANSWER 1 OF 158  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:666025  CAPLUS
DOCUMENT NUMBER:          145:152690
TITLE:                    Method for inducing crystalline state transition in
                          pharmaceuticals
INVENTOR(S):              Nakamichi, Kouichi; Izumi, Shougo; Oka, Masaaki
PATENT ASSIGNEE(S):       Nippon Shinyaju Company, Ltd., Japan
SOURCE:                   U.S., 18 pp., Cont.-in-part of U. S. 5,456,923.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
```

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5811547	A	19980922	US 1995-416815	19950609 <--
CA 2147279	A1	19940428	CA 1993-2147279	19931013 <--
WO 9408561	A1	19940428	WO 1993-JP1469	19931013 <--
W: AU, BR, CA, FI, HU, JP, KR, NO, NZ, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9351607	A	19940509	AU 1993-51607	19931013 <--
EP 665009	A1	19950802	EP 1993-922625	19931013 <--
EP 665009	B1	20000216		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 189770	T	20000315	AT 1993-922625	19931013 <--
ES 2145063	T3	20000701	ES 1993-922625	19931013 <--
US 5456923	A	19951010	US 1993-129133	19931115 <--

PRIORITY APPLN. INFO.:

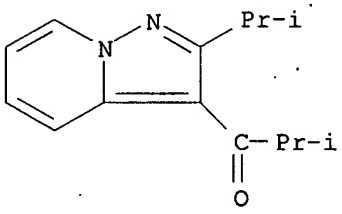
JP 1992-303085	A	19921014
WO 1993-JP1469	W	19931013
US 1993-129133	A2	19931115
JP 1991-112554	A	19910416
WO 1992-JP470	W	19920414

AB This invention has for its object to provide a method of inducing a transition in crystalline state of a crystallizable pharmaceutical with great ease and improved efficiency and uniformity on a high production scale. An extruder is used for inducing a transition from one crystalline state (Δ) to another crystalline state in a crystallizable pharmaceutical. An extruded indomethacin (form α) was converted to an amorphous form.

IT 50847-11-5, Ibudilast
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for inducing crystalline state transition in pharmaceuticals)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 158 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:296061 CAPLUS
DOCUMENT NUMBER: 138:297701
TITLE: Transmucosal administration of phosphodiesterase inhibitors for the treatment of erectile dysfunction
INVENTOR(S): Doherty, Paul C., Jr.; Place, Virgil A.; Smith, William L.
PATENT ASSIGNEE(S): Vivus, Inc., USA
SOURCE: U.S., 13 pp., Cont.-in-part of U.S. 6,037,346.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6548490	B1	20030415	US 1999-467094	19991210
US 6037346	A	20000314	US 1998-181070	19981027 <--
CA 2394060	A1	20010614	CA 2000-2394060	20001208 <--
WO 2001041807	A2	20010614	WO 2000-US33372	20001208 <--
WO 2001041807	A3	20020214		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 200122566	A	20010618	AU 2001-22566	20001208 <--
EP 1237577	A2	20020911	EP 2000-986297	20001208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003516363	T	20030513	JP 2001-543151	20001208
US 2002037828	A1	20020328	US 2001-888250	20010621
US 6403597	B2	20020611		
US 2002004498	A1	20020110	US 2001-938417	20010823
US 2003134861	A1	20030717	US 2003-351198	20030124
AU 2005248938	A1	20060202	AU 2005-248938	20051223

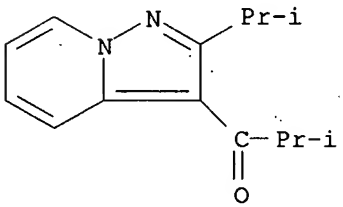
PRIORITY APPLN. INFO.:	US 1997-958816	B2 19971028
	US 1998-181070	A2 19981027
	US 1999-467094	A 19991210
	AU 2001-22566	A3 20001208
	WO 2000-US33372	W 20001208

AB A method is provided for treating erectile dysfunction in a mammalian male individual. The method involves the transmucosal administration of a phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or derivative thereof, within the context of an effective dosing regimen. Preferred modes of administration include transbuccal, sublingual and transrectal routes. Pharmaceutical formulations and kits are provided as well.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transmucosal administration of phosphodiesterase inhibitors for the treatment of erectile dysfunction)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 158 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:241329 CAPLUS

DOCUMENT NUMBER: 136:284433
TITLE: Administration of phosphodiesterase inhibitors for the treatment of premature ejaculation
INVENTOR(S): Wilson, Leland F.; Doherty, Paul C.; Place, Virgil A.; Smith, William L.; Abdel-Hamid, Abdou Ali Ibrahim Aboubakr
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 467,094.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002037828	A1	20020328	US 2001-888250	20010621
US 6403597	B2	20020611		
US 6037346	A	20000314	US 1998-181070	19981027 <--
US 6548490	B1	20030415	US 1999-467094	19991210
CA 2451152	A1	20030103	CA 2002-2451152	20020325
WO 2003000343	A2	20030103	WO 2002-US9415	20020325
WO 2003000343	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002248712	A1	20030108	AU 2002-248712	20020325
EP 1418896	A2	20040519	EP 2002-717729	20020325
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005519851	T	20050707	JP 2003-506984	20020325
AU 2005248938	A1	20060202	AU 2005-248938	20051223

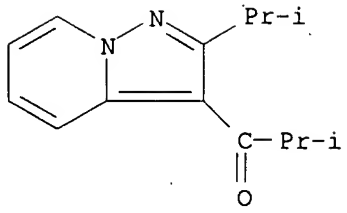
PRIORITY APPLN. INFO.:

US 1997-958816	B2	19971028
US 1998-181070	A2	19981027
US 1999-467094	A2	19991210
AU 2001-22566	A3	20001208
US 2001-888250	A	20010621
WO 2002-US9415	W	20020325

AB A method is provided for treatment of premature ejaculation by administration of a phosphodiesterase inhibitor, e.g., an inhibitor of a Type III, Type IV, or Type V phosphodiesterase. In a preferred embodiment, administration is on as "as needed" basis, i.e., the drug is administered immediately or several hours prior to sexual activity. Pharmaceutical formulations and packaged kits are also provided. Zaprinast 1.0, mannitol 1.0, microcryst. cellulose 2.0, and magnesium stearate 10 mg are blended in a suitable mixer and then compressed into sublingual tablets. Each sublingual tablet contains 10 mg zaprinast.

IT 50847-11-5, Ibudilast
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration of phosphodiesterase inhibitors for treatment of premature ejaculation)

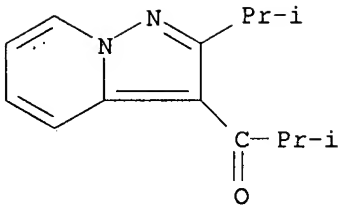
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L5 ANSWER 4 OF 158 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:41645 CAPLUS
DOCUMENT NUMBER: 137:118839
TITLE: Ibudilast: a non-selective PDE inhibitor with multiple actions on blood cells and the vascular wall
AUTHOR(S): Kishi, Yukio; Ohta, Seiko; Kasuya, Natsuko; Sakita, Shinya; Ashikaga, Takashi; Isobe, Mitsuaki
CORPORATE SOURCE: Department of Cardiovascular Medicine, Tokyo Medical and Dental University, Tokyo, 113-8519, Japan
SOURCE: Cardiovascular Drug Reviews (2001), 19(3), 215-225
CODEN: CDREEA; ISSN: 0897-5957
PUBLISHER: Neva Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Ibudilast (3-isobutyryl-2-isopropylpyrazolo[1,5-a]pyridine) is a nonselective inhibitor of cyclic nucleotide phosphodiesterase (PDE). It is widely used in Japan for improving prognosis and relieving symptoms in patients suffering from ischemic stroke or bronchial asthma. These clin. applications are based on the properties of ibudilast that inhibit platelet aggregation, improve cerebral blood flow and attenuate allergic reactions. The inhibition of platelet aggregation and vasodilatation by ibudilast may be due to synergistic elevation of intracellular cyclic nucleotides and release of nitric oxide (NO) or prostacyclin from endothelium, rather than direct inhibition of PDE5 or PDE3. Another important property of ibudilast is its antiinflammatory activity possibly associated with potent inhibition of PDE4. Combined with its relaxing effects on bronchial smooth muscle, antiinflammatory activity of ibudilast could favorably influence pathophysiol. of asthma by antagonizing chemical mediators triggering asthmatic attacks. Ibudilast was also reported to significantly attenuate inflammatory cell infiltration in the lumbar spinal cord in an animal model of encephalomyelitis. Future investigations should include effects of ibudilast on inflammatory reactions between endothelium and blood cells, which may initiate the development of atherosclerosis.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ibudilast as a nonselective PDE inhibitor with multiple actions on blood cells and vascular wall)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

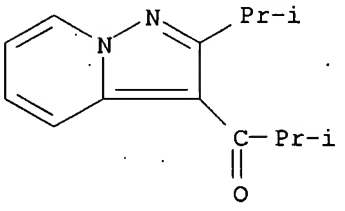
L5 ANSWER 5 OF 158 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:791880 CAPLUS
DOCUMENT NUMBER: 135:348877
TITLE: Cooling agents containing caffeine derivatives for pharmaceutical composition
INVENTOR(S): Matsushima, Hiroaki; Okumura, Shigetoshi; Morioka, Shigeo
PATENT ASSIGNEE(S): Rohto Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001302545	A	20011031	JP 2001-39116	20010215 <--
PRIORITY APPLN. INFO.:			JP 2000-36557 A	20000215

OTHER SOURCE(S): MARPAT 135:348877

AB The invention relates to a method for refrigerating a composition, especially mucosal pharmaceutical composition, without causing unwanted sensory, e.g. unwanted odor and irritation, wherein the composition contains caffeine, theophylline, diprophylline, theobromine, proxyphylline, pentoxifylline, and/or related compound An eye drop containing caffeine anhydride 3, tetrahydrozoline hydrochloride 0.5, neostigmine methylsulfate 0.05, pyridoxin hydrochloride 1, potassium aspartate 10, benzalchonium chloride 0.1, boric acid 5, NaOH q.s., and water q.s. to 1000 mL was formulated.

IT 50847-11-5, Ibudilast
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mucosal compns. containing active agents and cooling agents containing caffeine derivs.)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L5 ANSWER 6 OF 158 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:788822 CAPLUS

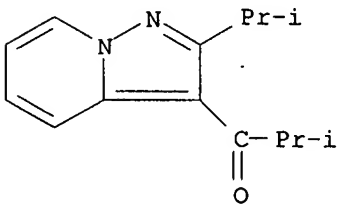
DOCUMENT NUMBER: 135:348876
TITLE: Method and agents for sensory improvement due to cooling agents
INVENTOR(S): Matsushima, Hiroaki; Okumura, Shigetoshi
PATENT ASSIGNEE(S): Rohto Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001302518	A	20011031	JP 2001-39117	20010215 <--
PRIORITY APPLN. INFO.:			JP 2000-36556 A	20000215

OTHER SOURCE(S): MARPAT 135:348876

AB The invention relates to a method for improving sensory, e.g. irritation, due to cooling agent, e.g. menthol, camphor, and borneol, etc., used in a composition, especially a mucosal composition, wherein the method includes addition of caffeine, theophylline, diprophylline, theobromine, proxyphylline, pentoxifylline, and/or related compound in the composition An eye drop containing caffeine anhydride 1, l-menthol 0.02, NaCl 0.8, KCl 0.15, polysorbate 80, sodium dihydrogen phosphate 0.2, sodium chondroitin sulfate 0.1, borax 0.16, benzalkonium chloride 0.004 g, and water and pH adjusting agent q.s. to 100 mL was formulated.

IT 50847-11-5, Ibudilast
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mucosal compns. containing active agents and cooling agents and sensory-improving agents)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



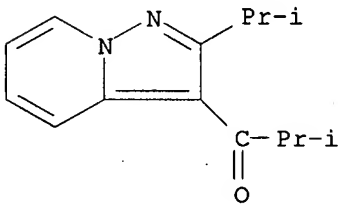
L5 ANSWER 7 OF 158 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:561569 CAPLUS
DOCUMENT NUMBER: 135:338959
TITLE: Ibudilast attenuates astrocyte apoptosis via cyclic GMP signalling pathway in an in vitro reperfusion model
AUTHOR(S): Takuma, K.; Lee, E.; Enomoto, R.; Mori, K.; Baba, A.; Matsuda, T.
CORPORATE SOURCE: Department of Analytical Chemistry, Kobe Gakuin University, Kobe, 651-2180, Japan
SOURCE: British Journal of Pharmacology (2001), 133(6), 841-848
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1 We examined the effect of 3-isobutyryl-2-isopropylpyrazolo[1,5-a]pyridine (ibudilast), which has been clin. used for bronchial asthma and cerebrovascular disorders, on cell viability induced in a model of reperfusion injury. 2 Ibudilast at 10-100 μM significantly attenuated the H2O2-induced decrease in cell viability. 3 Ibudilast inhibited the H2O2-induced cytochrome c release, caspase-3 activation, DNA ladder formation and nuclear condensation, suggesting its anti-apoptotic effect. 4 Phosphodiesterase inhibitors such as theophylline, pentoxyfylline, vinpocetine, dipyridamole and zaprinast, which increased the guanosine-3',5'-cyclic monophosphate (cGMP) level, and dibutyryl cGMP attenuated the H2O2-induced injury in astrocytes. 5 Ibudilast increased the cGMP level in astrocytes. 6 The cGMP-dependent protein kinase inhibitor KT5823 blocked the protective effects of ibudilast and dipyridamole on the H2O2-induced decrease in cell viability, while the cAMP-dependent protein kinase inhibitor KT5720, the cAMP antagonist Rp-cyclic AMPS, the mitogen-activated protein/extracellular signal-regulated kinase inhibitor PD98059 and the leukotriene D4 antagonist LY 171883 did not. 7 KT5823 also blocked the effect of ibudilast on the H2O2-induced cytochrome c release and caspase-3-like protease activation. 8 These findings suggest that ibudilast prevents the H2O2-induced delayed apoptosis of astrocytes via a cGMP, but not cAMP, signaling pathway.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ibudilast attenuates rat astrocyte apoptosis via a cyclic GMP, but not a cAMP, signaling pathway in an in vitro reperfusion model)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 158 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:434902 CAPLUS
DOCUMENT NUMBER: 135:51053
TITLE: Transmucosal administration of phosphodiesterase inhibitors for the treatment of erectile dysfunction
INVENTOR(S): Doherty, Paul C., Jr.; Place, Virgil A.; Smith, William L.
PATENT ASSIGNEE(S): Vivus, Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001041807	A2	20010614	WO 2000-US33372	20001208 <--

WO 2001041807	A3	20020214			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6548490	B1	20030415	US 1999-467094	19991210	
CA 2394060	A1	20010614	CA 2000-2394060	20001208	<--
AU 200122566	A	20010618	AU 2001-22566	20001208	<--
EP 1237577	A2	20020911	EP 2000-986297	20001208	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003516363	T	20030513	JP 2001-543151	20001208	
AU 2005248938	A1	20060202	AU 2005-248938	20051223	

PRIORITY APPLN. INFO.:

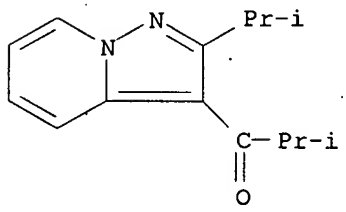
US 1999-467094	A	19991210
US 1997-958816	B2	19971028
US 1998-181070	A2	19981027
AU 2001-22566	A3	20001208
WO 2000-US33372	W	20001208

AB A method is provided for treating erectile dysfunction in a mammalian male individual. The method involves the transmucosal administration of a phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or derivative thereof, within the context of an effective dosing regimen. Preferred modes of administration include transbuccal, sublingual and transrectal routes. Pharmaceutical formulations and kits are provided as well. Thus, a buccal dosage form was prepared from 10 g sildenafil citrate and 90 g gelatin. After the mixing was complete, 20 g concentrated glycerin, 10 g lactose and 20 g mannitol were added and the components were mixed until uniform. Aliquot portions (150 mg) of the mixture were compression-molded to provide a buccal dosage unit. Each buccal unit contained 10 mg sildenafil citrate.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transmucosal administration of phosphodiesterase inhibitors for treatment of erectile dysfunction)

RN 50847-11-5 CAPLUS

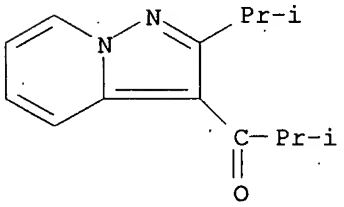
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L5 ANSWER 9 OF 158 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2001:351396 CAPLUS
DOCUMENT NUMBER:	135:147152
TITLE:	Potentiation of Ibudilast Inhibition of Platelet Aggregation in the Presence of Endothelial Cells
AUTHOR(S):	Rile, G.; Yatomi, Y.; Qi, R.; Satoh, K.; Ozaki, Y.
CORPORATE SOURCE:	Department of Clinical and Laboratory Medicine,

Yamanashi Medical University, Tamaho, Nakakoma, Yamanashi, 409-3898, Japan
SOURCE: Thrombosis Research (2001), 102(3), 239-246
CODEN: THBRAA; ISSN: 0049-3848
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although communications between platelets and endothelial cells or other blood cells are important in in vivo thrombus formation, laboratory platelet function tests are usually performed in isolation from these surrounding cells. In this study, we evaluated the effect of an antiplatelet drug, ibudilast (3-isobutyryl-2-isopropylpyrazolo[1,5-a]pyridine), on platelet aggregation in the presence and absence of human umbilical vein endothelial cells (HUVECs) and with the use of platelet-rich plasma (PRP) or whole blood as platelet samples. Stimulation-dependent platelet aggregation was weakened in the presence of HUVECs, which was especially prominent when the thrombin receptor-activating peptide SFLL (compared with ADP and epinephrine) was used as an aggregating agent. Ibudilast hardly affected SFLL-induced platelet aggregation (in PRP), while this antiplatelet agent was found to clearly inhibit this SFLL-induced response in a concentration-dependent manner, in the presence of HUVECs. Ibudilast tended to inhibit ADP- or epinephrine-induced platelet aggregation in the presence of HUVECs, but the effects were not statistically significant. Enhanced inhibition by ibudilast of SFLL-induced platelet aggregation (in the presence of HUVECs) was reproduced with the use of whole blood samples when a screen filtration pressure method was employed. It is suggested that the platelet aggregation studies in the presence of endothelial cells and/or other blood cells provide us with valuable information on platelet reactivity in vivo and improvement of antiplatelet therapy.
IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(potentiation of ibudilast inhibition of platelet aggregation in presence of endothelial cells)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 158 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:152681 CAPLUS
DOCUMENT NUMBER: 134:193444
TITLE: Preparation of imidazo[1,2-a]pyridinylpyrimidines and pyrazolo[2,3-a]pyridinylpyrimidines as inhibitors of CDK2, CDK4, and CDK6 cell cycle kinases.
INVENTOR(S): Thomas, Andrew Peter; Breault, Gloria Anne; Beattie, John Franklin; Jewsbury, Phillip John
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014375	A1	20010301	WO 2000-GB3139	20000815 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2376293	A1	20010301	CA 2000-2376293	20000815 <--
BR 2000013476	A	20020430	BR 2000-13476	20000815
EP 1214318	A1	20020619	EP 2000-953319	20000815
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HU 200202494	A2	20021028	HU 2002-2494	20000815
JP 2003507478	T	20030225	JP 2001-518706	20000815
AU 757639	B2	20030227	AU 2000-65833	20000815
EE 200200080	A	20030616	EE 2002-80	20000815
AT 251623	T	20031015	AT 2000-953319	20000815
PT 1214318	T	20040227	PT 2000-953319	20000815
ES 2208397	T3	20040616	ES 2000-953319	20000815
NZ 516740	A	20040924	NZ 2000-516740	20000815
RU 2248976	C2	20050327	RU 2002-107128	20000815
ZA 2002000028	A	20030402	ZA 2002-28	20020102
IN 2002MN00027	A	20050318	IN 2002-MN27	20020109
BG 106383	A	20020930	BG 2002-106383	20020204
NO 2002000832	A	20020412	NO 2002-832	20020220
NO 322818	B1	20061211		
US 6855719	B1	20050215	US 2002-69019	20020221
HK 1045510	A1	20040319	HK 2002-107002	20020925

PRIORITY APPLN. INFO.: GB 1999-19778 A 19990821
WO 2000-GB3139 W 20000815

OTHER SOURCE(S): MARPAT 134:193444
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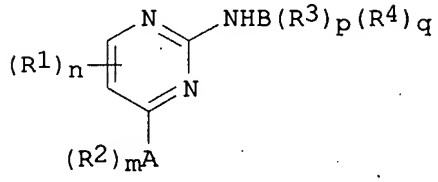


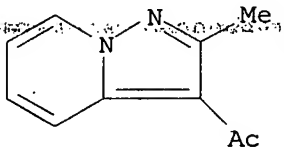
I

AB Title compds. [I; A = imidazo[1,2a]pyrid-3-yl, pyrazolo[2,3a]pyrid-3-yl; R1 = halo, NO2, cyano, OH, CF3, OCF3, amino, CO2H, sulfamoyl, (substituted) alkyl, alkenyl, alkynyl, alkoxy, alkanoyl, alkanoyloxy, Ph, heterocyclyl, etc.; R2 = halo, NO2, cyano, OH, CF3, OCF3, amino, CO2H, SH, carbamoyl, sulfamoyl, (substituted) alkyl, alkenyl, alkynyl, alkoxyl, Ph, heterocyclyl, PhS, etc.; R3 = halo, NO2, cyano, OH, amino, CO2H, carbamoyl, SH, sulfamoyl, alkenyl, alkynyl; m = 0-5; n = 0-2; Ring B = Ph or Ph fused to a C5-7 cycloalkyl ring; p = 0-4; R4 = AE; A = (substituted) alkyl, Ph, heterocyclyl, cycloalkyl, phenylalkyl, heterocyclylalkyl, cycloalkylcycloalkyl; E = bond, O, CO, CO2, NRaCO, NRa, S, SO, SO2,

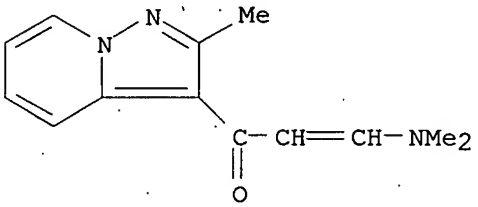
SO2NRa; q = 0-2; p+q≤5], were prepared Thus, NaH was added to 3-chloroaniline in N-methylpyrrolidone; after 30 min. 4-(2-methylimidazo[1,2-a]pyridin-3-yl)-2-methylthiopyrimidine (preparation given) in N-methylpyrrolidone was added and the mixture was heated at 150° for 3 h to give 21% 2-(3-chloroanilino)-4-(2-methylimidazo[1,2-a]pyrid-3-yl)pyrimidine. 2-[4-(2-Diethylaminoethoxy)anilino]-4-(imidazo[1,2-a]pyrid-3-yl)pyrimidine showed CDK2 inhibitory activity with IC50 = 0.17 μM.

IT 17408-29-6P 328064-17-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of imidazo[1,2-a]pyridinylpyrimidines and pyrazolo[2,3-a]pyridinylpyrimidines as inhibitors of CDK2, CDK4, and CDK6 cell cycle kinases)

RN 17408-29-6 CAPLUS
CN Ethanone, 1-(2-methylpyrazolo[1,5-a]pyridin-3-yl)- (9CI) (CA INDEX NAME)



RN 328064-17-1 CAPLUS
CN 2-Propen-1-one, 3-(dimethylamino)-1-(2-methylpyrazolo[1,5-a]pyridin-3-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

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         27669 PHOSPHODIESTERAS?
L6          44 L4 AND PHOSPHODIESTERAS?

=> s l6 and inhibit?
       1943847 INHIBIT?
L7          44 L6 AND INHIBIT?

=> d ibib abs hitstr tot

L7   ANSWER 1 OF 44  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2007:537700  CAPLUS
DOCUMENT NUMBER:         146:507686
TITLE:                   Pharmaceutical combination comprising atorvastatin
                         derivatives
INVENTOR(S):             Sattigeri, Jitendra A.; Bansal, Vinay S.
```

PATENT ASSIGNEE(S): Ranbaxy Laboratories Ltd., India
SOURCE: PCT Int. Appl., 46pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007054789	A1	20070518	WO 2006-IB3152	20061108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

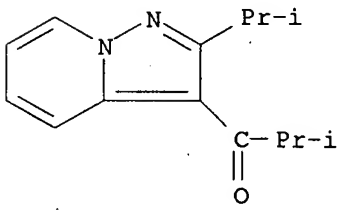
IN 2005-DE2964	A	20051108
IN 2005-DE2967	A	20051108
IN 2005-DE3033	A	20051114

OTHER SOURCE(S): MARPAT 146:507686

AB This invention relates to a combination product or medicament comprising at least one novel substituted pyrrole derivative and one or more dyslipidemia agents, antiobesity agents, antihyperglycemic agents, anti-inflammatory agents or mixture thereof. Also provided herein are the pharmaceutical compns. comprising at least one novel substituted pyrrole derivative and one or more dyslipidemic agents, antiobesity agents, antihyperglycemic agents, anti-inflammatory agents or mixture thereof and optionally together with at least one pharmaceutically acceptable carrier, and methods for the treatment or prophylaxis of cardiovascular diseases, Alzheimer's disease, obesity, diabetes or inflammatory diseases comprising administering to a mammal in need thereof therapeutically effective amts. of combination pharmaceutical composition comprising at least one novel substituted pyrrole derivative and one or more dyslipidemic agents, antiobesity agents, antihyperglycemic agents, anti-inflammatory agents or mixts. thereof.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combination comprising atorvastatin derivs.)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:464406 CAPLUS
DOCUMENT NUMBER: 146:435235
TITLE: Phosphodiesterase (PDE) agents for modulation of neurogenesis, combinations with other agents, and therapeutic use
INVENTOR(S): Barlow, Carrolee; Carter, Todd A.; Lorrain, Kym I.; Pires, Jammieson C.; Treuner, Kai
PATENT ASSIGNEE(S): Braincells, Inc., USA
SOURCE: PCT Int. Appl., 99pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007047978	A2	20070426	WO 2006-US41131	20061020

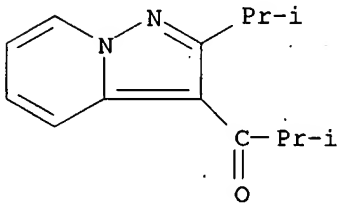
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-729366P P 20051021
US 2006-784605P P 20060321
US 2006-807594P P 20060717

AB The invention discloses methods for treating diseases and conditions of the central and peripheral nervous system by stimulating or increasing neurogenesis. The invention includes compns. and methods based on use of a PDE agent, optionally in combination with one or more other neurogenic agents, to stimulate or activate the formation of new nerve cells.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase agents for modulation of neurogenesis, combinations with other agents, and therapeutic use)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 3 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:410817 CAPLUS
DOCUMENT NUMBER: 146:408426
TITLE: Antiscarring drug combinations
INVENTOR(S): Hunter, William L.; Toleikis, Philip M.; Gravett,

David M.; Grau, Daniel S.; Borisy, Alexis; Keith, Curtis T.; Auspitz, Benjamin A.; Nichols, M. James; Jost-Price, Edward Roydon; Serbedzija, George N.

PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA; Angiotech International AG
SOURCE: PCT Int. Appl., 1032pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007041593	A2	20070412	WO 2006-US38675	20061003

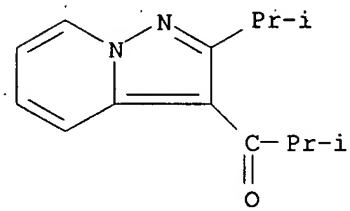
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-723053P P 20051003

AB The present invention provides devices or implants that comprise antiscarring drug combinations, methods or making such devices or implants, and methods of inhibiting fibrosis between the devices or implants and tissue surrounding the devices or implants. The present invention also provides compns. that comprise anti-fibrotic drug combinations, and their uses in various medical applications including the prevention of surgical adhesions, treatment of inflammatory arthritis, treatment of scars and keloids, the treatment of vascular disease, and the prevention of cartilage loss. Combinations containing 0.03 or 0.1 mg/kg methylprednisolone acetate (I) with higher amoxapine doses of 2.26 mg/kg significantly enhanced I effects, bringing down the edema levels to 13.6 and 12,5%, resp. This is equivalent to the effect observed using Depo-Medrol, but with a much lower steroid dose.

IT 50847-11-5, Ibudilast 852804-82-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiscarring drug combinations)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



RN 852804-82-1 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-, mixt. with 2,2',2'',2'''-[(4,8-di-1-piperidinylpyrimido[5,4-d]pyrimidine-2,6-diyl)dinitrilo]tetrakis[ethanol] (9CI) (CA INDEX NAME)

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CRN 50847-11-5
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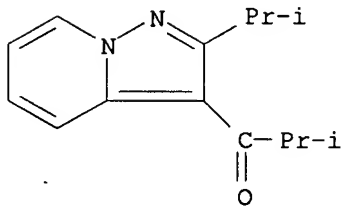
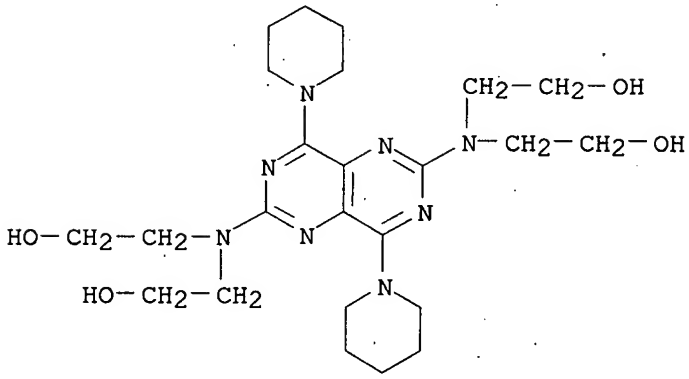


CM 2

CRN 58-32-2
CMF C24 H40 N8 O4



L7 ANSWER 4 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:410754 CAPLUS
DOCUMENT NUMBER: 146:408504
TITLE: Soft tissue implants and drug combination compositions
INVENTOR(S): Hunter, William L.; Toleikis, Philip M.; Gravett, David M.; Grau, Daniel S.; Borisy, Alexis; Keith, Curtis T.; Auspitz, Bnjamin A.; Nichols, M. James; Jost-Price, Edward Roydon; Serbedzija, George N.
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA; Angiotech International AG
SOURCE: PCT Int. Appl., 677pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007041677	A2	20070412	WO 2006-US38957	20061003
WO 2007041677	A9	20070531		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,

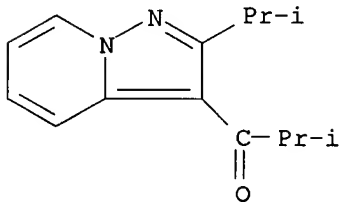
MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-723601P P 20051003

AB Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and nasal implants) are used in combination with an anti-scarring drug combination in order to inhibit scarring that may otherwise occur when the implant is placed within an animal. Combinations containing 0.03 or 0.1 mg/kg methylprednisolone acetate (I) with higher amoxapine doses of 2.26 mg/kg significantly enhanced I effects, bringing down the edema levels to 13.6 and 12,5%, resp. This is equivalent to the effect observed using Depo-Medrol, but with a much lower steroid dose.

IT 50847-11-5, Ibudilast 852804-82-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soft tissue implants and drug combination compns.)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-
(CA INDEX NAME)



RN 852804-82-1 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-,
mixt. with 2,2',2'',2'''-[(4,8-di-1-piperidinylpyrimido[5,4-d]pyrimidine-
2,6-diyl)dinitrilo]tetrakis[ethanol] (9CI) (CA INDEX NAME)

CM 1

CRN 50847-11-5
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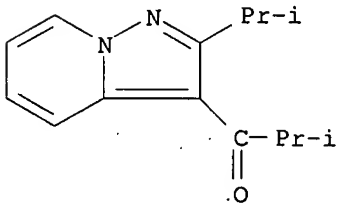
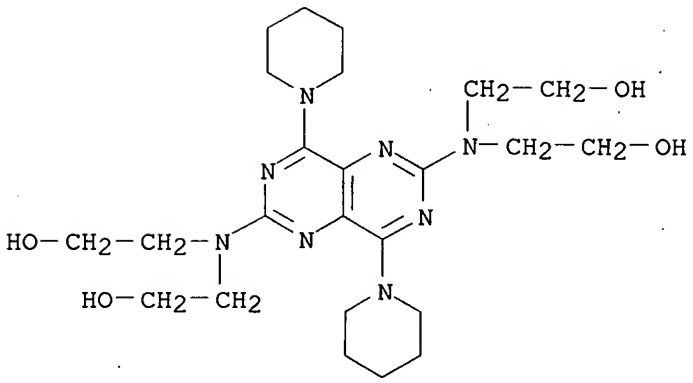


CM 2

CRN 58-32-2
CMF C24 H40 N8 O4



L7 ANSWER 5 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:410705 CAPLUS
DOCUMENT NUMBER: 146:408424
TITLE: Implantable sensors, implantable pumps, and anti-scarring drug combinations
INVENTOR(S): Hunter, William L.; Toleikis, Philip M.; Gravett, David M.; Grau, Daniel S.; Borisy, Alexis; Keith, Curtis T.; Auspitz, Benjamin A.; Nichols, M. James; Jost-Price, Edward Roydon; Serbedzija, George N.
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA; Angiotech International A.-G.
SOURCE: PCT Int. Appl., 713pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007041584	A2	20070412	WO 2006-US38632	20061003

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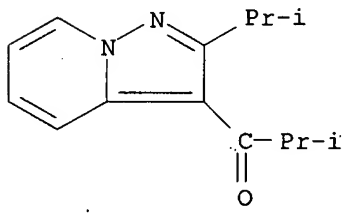
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-723638P P 20051003

AB Pumps and sensors for contact with tissue are used in combination with an anti-scarring agent or a composition that comprises an anti-scarring agent to inhibit scarring that may otherwise occur when the pumps and sensors are implanted within an animal. Combinations containing 0.03 or 0.1 mg/kg methylprednisolone acetate (I) with higher amoxapine doses of 2.26 mg/kg significantly enhanced I effects, bringing down the edema levels to 13.6 and 12,5%, resp. This is equivalent to the effect observed using Depo-Medrol, but with a much lower steroid dose.

IT 50847-11-5, Ibudilast 852804-82-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable sensors and implantable pumps and anti-scarring drug combinations)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



RN 852804-82-1 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-, mixt. with 2,2',2'',2'''-[(4,8-di-1-piperidinylpyrimido[5,4-d]pyrimidine-2,6-diyl)dinitrilo]tetrakis[ethanol] (9CI) (CA INDEX NAME)

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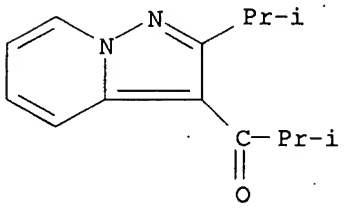
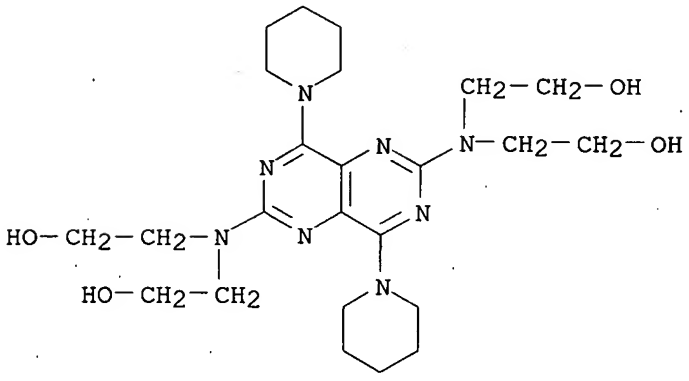
CRN 50847-11-5
CMF C14 H18 N2 O



CM 2

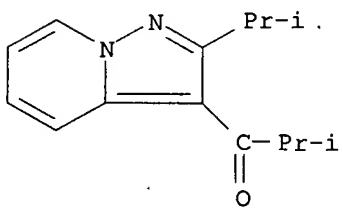
CRN 58-32-2
CMF C24 H40 N8 O4



L7 ANSWER 6 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1090008 CAPLUS
DOCUMENT NUMBER: 146:140600
TITLE: New therapeutic agents against multiple sclerosis
AUTHOR(S): Suzumura, Akio
CORPORATE SOURCE: Department of Neuroimmunology, Research Institute of

Environmental Medicine, Nagoya University, Furo-cho, Chikusa-ku, Nagoya, 464-8601, Japan
SOURCE: Shinkei Kenkyu no Shinpo (2006), 50(4), 644-651
CODEN: SKNSAF; ISSN: 0001-8724
PUBLISHER: Igaku Shoin Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. Interferon-β (IFNβ) is now widely used for the treatment of multiple sclerosis (MS). However, because of the side-effects and poor-responsiveness, not all the patients with MS take advantage with IFNβ treatment. In addition, IFNβ dose not suppress all the pathol. processes of MS. Thus, the authors still need the new therapeutic strategy. To suppress pathophysiol. of MS, the authors have to develop the novel ways to protect neurons and to induce remyelination in addition to the immunosuppression. Statins and phosphodiesterase inhibitors are now examined for this purpose. In this review, I discuss the mechanisms of MS and possible candidates for future treatment of MS.

IT 50847-11-5, Ibudilast
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(new therapeutic agents against multiple sclerosis)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-
(CA INDEX NAME)



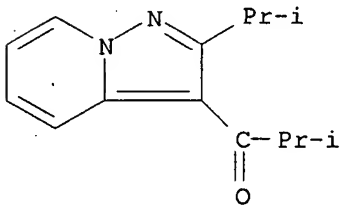
L7 ANSWER 7 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:409880 CAPLUS
DOCUMENT NUMBER: 144:425711
TITLE: Method and composition using an interferon-β-phosphodiesterase inhibitor
combination for the treatment of multiple sclerosis
INVENTOR(S): Suzumura, Akio
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006093578	A1	20060504	US 2005-266409		20051104
PRIORITY APPLN. INFO.:			US 2004-624851P	P	20041104

AB A method for treating multiple sclerosis includes administering interferon-β and a phosphodiesterase inhibitor in combination in a therapeutically effective amount

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interferon-β- phosphodiesterase inhibitor
combination for treatment of multiple sclerosis)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)

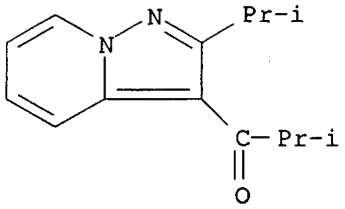


L7 ANSWER 8 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:382641 CAPLUS
DOCUMENT NUMBER: 145:20712
TITLE: Preferential inhibition of human phosphodiesterase 4 by ibudilast
AUTHOR(S): Huang, Zheng; Liu, Susana; Zhang, Lei; Salem, Myriam; Greig, Gillian M.; Chan, Chi Chung; Natsumeda, Yutaka; Noguchi, Kazuhito
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Kirkland, QC, Can.
SOURCE: Life Sciences (2006), 78(23), 2663-2668
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ibudilast ophthalmic solution exhibited an improved clin. efficacy over cromoglycate in the treatment of allergic conjunctivitis. To further characterize its principal mode of action, the phosphodiesterase (PDE) inhibitory profile of ibudilast has been examined using human recombinant enzymes. Ibudilast, but not the other commonly used anti-allergic ophthalmic solns. including cromoglycate, ketotifen, tranilast and levocabastine, potently inhibits purified human PDE4A, 4B, 4C and 4D with IC50 values at 54, 65, 239 and 166 nM, resp. Ibudilast effectively blocks lipopolysaccharide (LPS)-induced tumor necrosis factor (TNFα, IC50 = 6.2 μM) and N-formyl-Met-Leu-Phe (fMLP)-induced leukotriene (LT) B4 biosynthesis (IC50 = 2.5 μM) in human whole blood, which are 3 and 6-fold more potent than cilomilast, resp. The attenuated inflammatory and allergic responses from the potent and preferential PDE4 inhibition of ibudilast may have contributed significantly to its beneficial pharmacol. responses and distinguishes ibudilast from the other ophthalmic solns. in the treatment of ocular allergy.

IT 50847-11-5, Ibudilast
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-allergic ibudilast in ophthalmic solution preferentially inhibits human PDE 4)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:29433 CAPLUS
DOCUMENT NUMBER: 144:135217
TITLE: Pharmaceutical compositions containing bezafibrate and analogs and diflunisal and its analog for the treatment of metabolic disorders
INVENTOR(S): Lee, Margaret S.; Zimmerman, Grant R.; Finelli, Alyce Lynn; Grau, Daniel; Keith, Curtis; Nichols, M. James
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006004803	A1	20060112	WO 2005-US23030	20050629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005259864	A1	20060112	AU 2005-259864	20050629
CA 2571683	A1	20060112	CA 2005-2571683	20050629
EP 1781303	A1	20070509	EP 2005-768186	20050629
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
US 2006069161	A1	20060330	US 2005-171566	20050630
NO 2007000510	A	20070329	NO 2007-510	20070126

PRIORITY APPLN. INFO.:

US 2004-584380P	P	20040630
US 2005-649329P	P	20050202
WO 2005-US23030	W	20050629

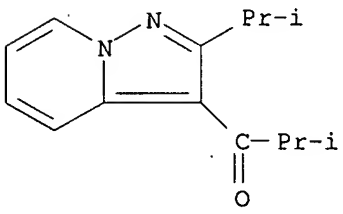
AB The invention features compns., methods, and kits for the treatment of metabolic disorders such as diabetes and obesity. For example, an oral composition containing combination of bezafibrate and diflunisal was found to be able to significantly increased the insulin-stimulated glucose uptake.

IT 50847-11-5, Ibudilast
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical compns. containing bezafibrate and analogs and diflunisal analogs or cinnamic acid for treatment of metabolic disorders)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:363641 CAPLUS

DOCUMENT NUMBER: 142:475665

TITLE: Anti-inflammatory therapy by ibudilast, a phosphodiesterase inhibitor, in demyelination of twitcher, a genetic demyelination model

AUTHOR(S): Kagitani-Shimono, Kuriko; Mohri, Ikuko; Fujitani, Yasushi; Suzuki, Kinuko; Ozono, Keiichi; Urade, Yoshihiro; Taniike, Masako

CORPORATE SOURCE: Department of Developmental Medicine (Pediatrics), Osaka University Graduate School of Medicine, Osaka, 565-0871, Japan

SOURCE: Journal of Neuroinflammation (2005), 2, No pp. given
CODEN: JNOEB3; ISSN: 1742-2094
URL: http://www.jneuroinflammation.com/content/pdf/1742-2094-2-10.pdf

PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

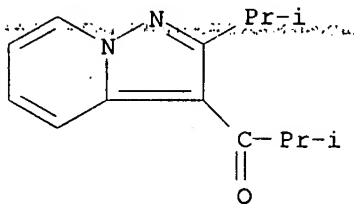
AB Background: Twitcher mouse (twi/twi) is an authentic murine model of Krabbe's disease. Accumulation of psychosine, resulting in apoptosis of oligodendrocytes and subsequent demyelination, is a cardinal event to the pathogenesis of this disease. Moreover, recruitment of inflammatory cells plays a significant role in the pathol. process in the twi/twi central and peripheral nervous systems. In this study, we investigated the (1) relationship between tumor necrosis factor-α (TNFα), pro-inflammatory cytokine, and the progression of this disease and (2) effect of the anti-inflammatory therapy by ibudilast, a phosphodiesterase inhibitor. Methods: We quantified the expression level of TNFα and TNF-receptor mRNA in twi/twi using semi-quant. RT-PCR. The relationship between TNFα expression, apoptosis of oligodendrocytes and demyelination was studied with immunohistochem. and TUNEL method. We then treated twi/twi with a daily i.p. injection of ibudilast (10mg/kg), which suppress TNFα production in the brain. Results: We found that TNFα-immunoreactive microglia/macrophages appeared in the twi/twi brain and that the mRNA levels of TNFα and TNF-receptor 1 was increased with the progression of demyelination. The distribution profile of TNFα-immunoreactive microglia/macrophages overlapped that of TUNEL-pos. oligodendrocytes in the twi/twi brain. When twi/twi was treated with ibudilast from PND30, the number of oligodendrocytes undergoing apoptosis was markedly reduced and demyelination was milder. Obvious improvement of clin. symptom was noted in two of five. The failure of constant clin. improvement by ibudilast may

result from hepatotoxicity and/or the inhibition of proliferation of NG2-pos. oligodendrocyte precursors. Conclusion: We conclude that anti-inflammatory therapy by a phosphodiesterase inhibitor can be considered as a novel alternative therapy for Krabbe's disease.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expression of tumor necrosis factor α and its receptor TNF-R1 in cerebellum was associated with demyelination in mouse model of Krabbe's disease which were inhibited by phosphodiesterase inhibitor ibudilast)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:347150 CAPLUS
DOCUMENT NUMBER: 142:386032
TITLE: Methods for treating diseases and conditions with G protein-coupled receptor inverse agonists and for screening for agents acting as inverse agonists
INVENTOR(S): Bond, Richard A.
PATENT ASSIGNEE(S): Inverseon, Inc., USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005035731	A2	20050421	WO 2004-US33530	20041008
WO 2005035731	A3	20060112		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004280638	A2	20050421	AU 2004-280638	20041008
AU 2004280638	A1	20050421		
CA 2544733	A1	20050421	CA 2004-2544733	20041008
EP 1684764	A2	20060802	EP 2004-794796	20041008

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

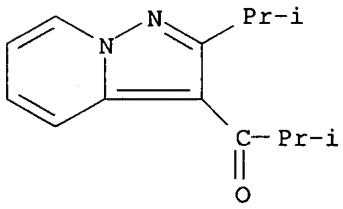
PRIORITY APPLN. INFO.: US 2003-510250P P 20031009
US 2004-555797P P 20040323
WO 2004-US33530 W 20041008

OTHER SOURCE(S): MARPAT 142:386032

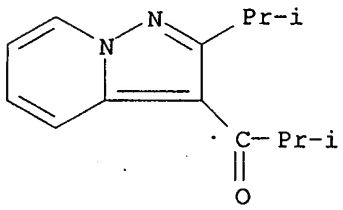
AB The invention describes a method for treating a disease or condition associated with the activity of a G protein-coupled receptor (GPCR) comprising administering an inverse agonist for the GPCR, alone or in combination with an agonist for the GPCR, to an organism with a disease or condition associated with the activity of the GPCR in a quantity and for a period that causes an increase in the population of spontaneously active GPCRs associated with that physiol. function, thereby producing a therapeutic effect to ameliorate the disease or condition. This provides a basis for so-called "paradoxical pharmacol." These methods can be used to treat pulmonary airway diseases, including asthma and chronic allergic rhinitis, among other diseases and conditions, including obesity. The invention further describes a screening method for screening a compound for inverse agonist activity to a GPCR.

IT 50847-11-5, Ibudilast 50847-11-5D, Ibudilast, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G protein-coupled receptor inverse agonists for disease treatment, and screening method)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 12 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:346808 CAPLUS
DOCUMENT NUMBER: 142:386003
TITLE: Method of treating airway diseases with beta-adrenergic inverse agonists
INVENTOR(S): Bond, Richard A.
PATENT ASSIGNEE(S): Inverseon, Inc., USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

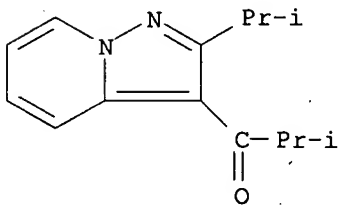
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005034871	A2	20050421	WO 2004-US33157	20041008
WO 2005034871	A3	20051124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004279438	A1	20050421	AU 2004-279438	20041008
AU 2004279438	A2	20050421		
CA 2544611	A1	20050421	CA 2004-2544611	20041008
EP 1677778	A2	20060712	EP 2004-809893	20041008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2006194882	A1	20060831	US 2005-264347	20051007
PRIORITY APPLN. INFO.:			US 2003-510250P P	20031009
			US 2004-555797P P	20040323
			WO 2004-US33157 W	20041008

OTHER SOURCE(S): MARPAT 142:386003

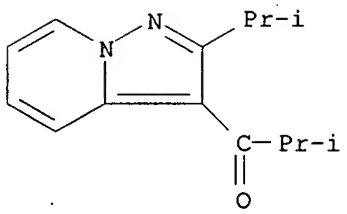
AB The use of β-adrenergic inverse agonists provides a new and highly efficient way of treating a number of pulmonary airway diseases, including asthma, emphysema, and chronic obstructive pulmonary diseases. In general, such a method comprises administering a therapeutically effective amount of a β-adrenergic inverse agonist to the subject to treat the pulmonary airway disease. Particularly preferred inverse agonists include nadolol and carvedilol.

IT 50847-11-5, Ibudilast 50847-11-5D, Ibudilast, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating airway diseases with beta-adrenergic inverse agonists)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)

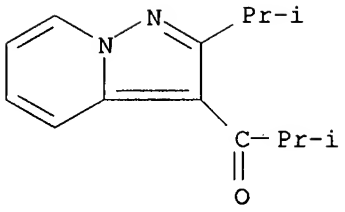


L7 ANSWER 13 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:12953 CAPLUS
DOCUMENT NUMBER: 142:309689
TITLE: Effect of ibudilast on learning and memory in rats with ligation of bilateral common carotid arteries
AUTHOR(S): Yamazaki, Takanobu; Masada, Kimiya; Yamanisi, Atsuhiro; Matsuzawa, Shigeki
CORPORATE SOURCE: Pharmacology, Research Department I, Research Center, Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: Japanese Pharmacology & Therapeutics (2004), 32(10), 647-653
CODEN: JPTABU
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB We examined the effect of ibudilast, a phosphodiesterase inhibitor, on impairment of learning and memory in rats with chronic cerebral hypoperfusion. Chronic cerebral hypoperfusion was induced by ligation of bilateral common carotid arteries in rats (2VO rats) under anesthesia. The vehicle (0.3% CMC) or ibudilast (10 and 30 mg/kg) was orally administered one hour before ligation, and thereafter once daily for 6 days. All evaluation or measurement was performed on the next day of the final administration (i.e., seven days after ligation). Parameters for evaluation were passive avoidance response and long-term potentiation (LTP). At the same time, hippocampal cAMP contents were measured as a biochem. parameter. Passive avoidance response and LTP were significantly impaired in these rats seven days after ligation compared with sham-operated rats. Seven-day treatment with ibudilast (30 mg/kg) significantly improved the impairment of passive avoidance response and LTP. Hippocampal cAMP contents tended to increase in the group treated with 30mg/kg of ibudilast, though not statistically significant from the control groups. When hippocampal tissues from rats treated with ibudilast (30 mg/kg) for seven days were incubated in the presence of forskolin, cAMP contents significantly increased, as compared with those from control rats. These results indicate that ligation of bilateral common carotid arteries induces behavioral and electro-pharmacol. impairment in rats, and that ibudilast improves this impairment. This suggests that chronic cerebral hypoperfusion could play an important role in development of dementia, and that ibudilast may be effective for dementia of this type.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of ibudilast on learning and memory in rats with ligation of bilateral common carotid arteries)

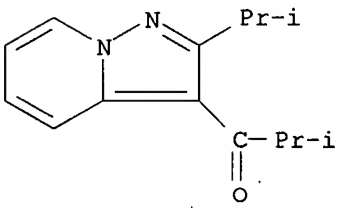
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 14 OF 44, CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:859846 CAPLUS
DOCUMENT NUMBER: 142:126945
TITLE: Ibudilast, a nonselective phosphodiesterase inhibitor, regulates Th1/Th2 balance and NKT cell subset in multiple sclerosis
AUTHOR(S): Feng, Juan; Misu, Tatsuro; Fujihara, Kazuo; Sakoda, Saburo; Nakatsuji, Yuji; Fukaura, Hikoaki; Kikuchi, Seiji; Tashiro, Kunio; Suzumura, Akio; Ishii, Naoto; Sugamura, Kazuo; Nakashima, Ichiro; Itoyama, Yasuto
CORPORATE SOURCE: Department of Neurology, Tohoku University School of Medicine, Aoba-ku, Sendai, 980-8574, Japan
SOURCE: Multiple Sclerosis (2004), 10(5), 494-498
CODEN: MUSCFZ; ISSN: 1352-4585
PUBLISHER: Arnold, Hodder Headline
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We investigated the immunoregulatory effects of ibudilast, a nonselective phosphodiesterase inhibitor, at a clin. applicable dose (60 mg/day p.o. for four weeks) in multiple sclerosis (MS) patients. Sensitive real-time PCR for quantifying cytokine mRNA in the blood CD4 + cells revealed that the ibudilast monotherapy significantly reduced tumor necrosis factor-α and interferon (IFN)-γ mRNA and the IFN-γ/interleukin-4 mRNA ratio, suggesting a shift in the cytokine profile from Th1 toward Th2 dominancy. In a flow cytometric anal., natural killer T cells, which have been reported to relate to Th2 responses in MS and its animal model (exptl. autoimmune encephalomyelitis), increased significantly after the therapy. None of the significant immunol. changes were seen in healthy subjects or untreated MS patients. Ibudilast may be a promising therapy for MS and its clin. effects warrant further study.

IT 50847-11-5, Ibudilast
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase inhibitor ibudilast immunoregulatory effects on Th1/Th2 cytokine balance and NKT cell subset in multiple sclerosis)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS

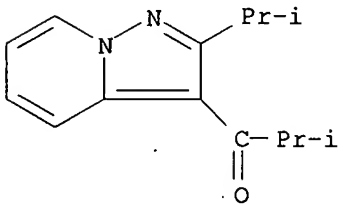
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:648390 CAPLUS
DOCUMENT NUMBER: 141:185092
TITLE: Combination of a phosphodiesterase IV (PDE IV) inhibitor and a tumor necrosis factor α (TNF-α) antagonist for the treatment of PDE IV-related conditions and TNF-α-related conditions
INVENTOR(S): Warner, James M.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004067006	A1	20040812	WO 2004-IB616		20040123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI					
US 2006083714	A1	20060420	US 2004-500266		20040618
PRIORITY APPLN. INFO.:			US 2003-442881P	P	20030127
			WO 2004-IB616	W	20040123

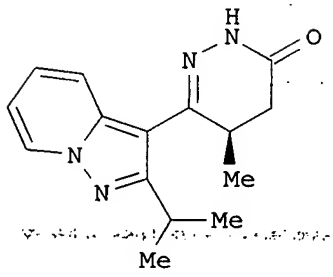
AB The invention discloses therapeutic combinations and methods for the treatment of inflammatory conditions and diseases. In particular, the invention discloses treatments and methods for PDE IV-related conditions and for TNF-α-related conditions using a combination of a PDE IV inhibitor and a TNF-α antagonist.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase IV inhibitor-tumor necrosis factor α antagonist combination for treatment of PDE IV-related conditions and TNF-α-related conditions)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 16 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:573012 CAPLUS
DOCUMENT NUMBER: 141:207153
TITLE: A short and efficient synthesis of a chiral pyridazinone derivative by the chiral-pool method
AUTHOR(S): Yoshida, Noriyuki; Awano, Katsuya; Kobayashi, Tomoshige; Fujimori, Kunihide
CORPORATE SOURCE: Research Center, Kyorin Pharmaceutical Co., Ltd.,

Nogi, 329-0114, Japan
SOURCE: Synthesis (2004), (10), 1554-1556
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:207153
GI



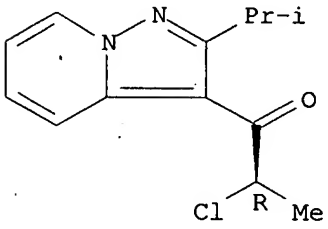
I

AB The asym. synthesis of a (R)-4,5-dihydro-5-methylpyridazin-3(2H)-one derivative bearing a pyrazolopyridine ring I, which is a potent inhibitor of phosphodiesterase, was achieved with a high optical yield in four steps starting from (R)-2-chloropropionyl chloride by a chiral-pool method.

IT 742104-09-2P 742104-10-5P 742104-11-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chiral pyridazinone derivative containing pyrazolopyridine ring in four steps starting from (R)-2-chloropropionyl chloride by chiral-pool method)

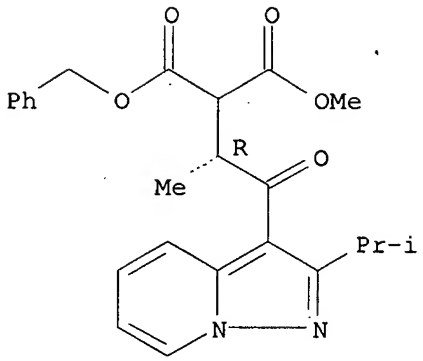
RN 742104-09-2 CAPLUS
CN 1-Propanone, 2-chloro-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



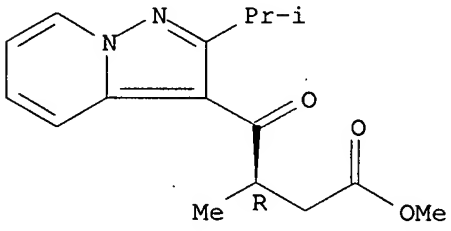
RN 742104-10-5 CAPLUS
CN Propanedioic acid, [(1R)-1-methyl-2-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-2-oxoethyl]-, methyl phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 742104-11-6 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, β-methyl-2-(1-methylethyl)-γ-oxo-, methyl ester, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



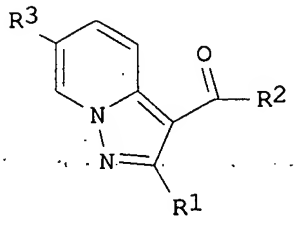
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:490726 CAPLUS
DOCUMENT NUMBER: 141:35467
TITLE: Ibudilast is a potent phosphodiesterase 10A inhibitor useful in treatment of neurological disorders
INVENTOR(S): Nagasawa, Michiaki; MacKenzie, Simon John
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050091	A1	20040617	WO 2003-JP15315	20031201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2508194	A1	20040617	CA 2003-2508194	20031201

AU 2003302588	A1	20040623	AU 2003-302588	20031201
EP 1570847	A1	20050907	EP 2003-812356	20031201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006106054	A1	20060518	US 2005-537313	20050928
PRIORITY APPLN. INFO.:			JP 2002-350804	A 20021203
			WO 2003-JP15315	W 20031201

GI



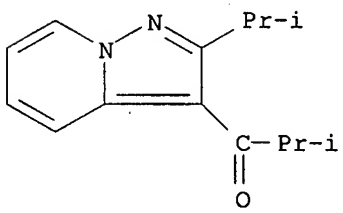
I

AB The invention provides phosphodiesterase 10A inhibitors containing, as the active ingredient, a pyrazolo[1,5-a]pyridine derivative represented by the following general formula (I): wherein R1 and R2 independently represent each hydrogen or C1-4 lower alkyl; and R3 represents hydrogen, C1-4 lower alkyl or C1-3 lower alkoxy. PDE10A inhibitors are useful in preventing or treating Parkinson's disease, Huntington's disease, Alzheimer's disease or schizophrenia. Ibudilast (3-isobutyryl-2-isopropylpyrazolo[1,5-a]pyridine) is a nonselective inhibitor of cyclic nucleotide phosphodiesterase (PDE) isoforms PDE3, PDE4, and PDE5. Here, the authors show that ibudilast is a potent inhibitor of phosphodiesterase 10A1 (PDE10A1), with IC50 of 3 and 1 μM for cAMP and cGMP reaction, resp.

IT 50847-11-5, Ibudilast
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ibudilast is a potent phosphodiesterase 10A inhibitor useful in treatment of neurol. disorders)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:126079 CAPLUS

DOCUMENT NUMBER: 140:314913

TITLE: Neuroprotective role of phosphodiesterase inhibitor ibudilast on neuronal cell death

induced by activated microglia

AUTHOR(S): Mizuno, Tetsuya; Kurotani, Tohru; Komatsu, Yukio; Kawanokuchi, Jun; Kato, Hideki; Mitsuma, Norimasa; Suzumura, Akio

CORPORATE SOURCE: Institute of Environmental Medicine, Department of Neuroimmunology, Nagoya University, Furo-cho, Chikusa-ku, Nagoya, 464-8601, Japan

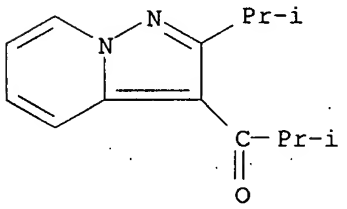
SOURCE: Neuropharmacology (2004), 46(3), 404-411
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The phosphodiesterase inhibitor, ibudilast, has many effects on lymphocytes, endothelial cells, and glial cells. We examined the neuroprotective role of ibudilast in neuron and microglia co-cultures. Ibudilast significantly suppressed neuronal cell death induced by the activation of microglia with lipopolysaccharide (LPS) and interferon (IFN)-γ. To examine the mechanisms by which ibudilast exerts a neuroprotective role against the activation of microglia, we examined the production of inflammatory and anti-inflammatory mediators and trophic factors following ibudilast treatment. In a dose-dependent manner, ibudilast suppressed the production of nitric oxide (NO), reactive oxygen species, interleukin (IL)-1β, IL-6, and tumor necrosis factor (TNF)-α and enhanced the production of the inhibitory cytokine, IL-10, and addnl. neurotrophic factors, including nerve growth factor (NGF), glia-derived neurotrophic factor (GDNF), and neurotrophin (NT)-4 in activated microglia. Thus, ibudilast-mediated neuroprotection was primarily due to the inhibition of inflammatory mediators and the upregulation of neurotrophic factor. In the CA1 region of hippocampal slices, long-term potentiation (LTP) induced by high frequency stimulation (HFS) could be inhibited with LPS and interferon-γ stimulation. Ibudilast returned this LTP inhibition to the levels observed in controls. These results suggest that ibudilast may be a useful neuroprotective and anti-dementia agent counteracting neurotoxicity in activated microglia.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective role of phosphodiesterase inhibitor ibudilast on neuronal cell death induced by activated microglia)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:1009432 CAPLUS

DOCUMENT NUMBER: 141:1136

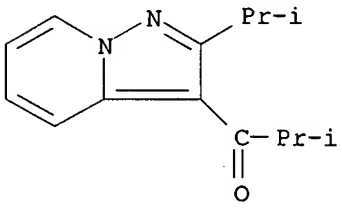
TITLE: Phosphodiesterase inhibitors suppress IL-12 production with microglia and T helper I development

AUTHOR(S): Suzumura, Akio; Ito, Atsushi; Mizuno, Tetsuya
CORPORATE SOURCE: Department of Neuroimmunology, Institute of Environmental Medicine, Nagoya University, Furo-cho, Chikusa, Nagoya, 464-8601, Japan
SOURCE: Multiple Sclerosis (2003), 9(6), 574-578
CODEN: MUSCFZ; ISSN: 1352-4585
PUBLISHER: Arnold, Hodder Headline
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of phosphodiesterase inhibitors (PDEIs) on interleukin (IL)-12 production by microglia, antigen-presenting cells in the central nervous system (CNS), were examined to learn how they affect T cell differentiation in the CNS. PDEIs significantly suppressed the microglial IL-12 production, as determined by reverse transcriptase-polymerase chain reaction for IL-12 p35 and p40 mRNA expression and by an ELISA specific for IL-12 functional heterodimer, p70. In addition, the PDEI ibudilast also suppressed interferon-γ, but not IL-4 or IL-10, production by myelin oligodendrocyte glycoprotein (MOG)-specific T cells reactivated with MOG in the presence of microglia. Thus, PDEIs may also suppress differentiation of T helper I (ThI) in the CNS. PDEIs can be of use for future therapeutic strategy to treat ThI -mediated diseases, such as multiple sclerosis.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase inhibitors effect on IL-12 production by microglia and T helper I development in CNS)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:864477 CAPLUS
DOCUMENT NUMBER: 140:157283
TITLE: Ibudilast, a phosphodiesterase inhibitor, protects against white matter damage under chronic cerebral hypoperfusion in the rat
AUTHOR(S): Wakita, Hideaki; Tomimoto, Hidekazu; Akiguchi, Ichiro; Lin, Jin-Xi; Ihara, Masafumi; Ohtani, Ryo; Shibata, Masunari
CORPORATE SOURCE: Faculty of Medicine, Department of Neurology, Kyoto University, Sakyo-ku, Kyoto, 606-8507, Japan
SOURCE: Brain Research (2003), 992(1), 53-59
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

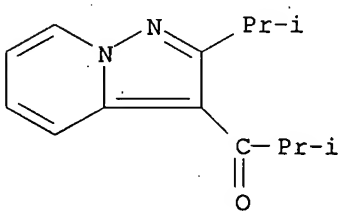
AB Cerebrovascular white matter (WM) lesions, which are frequently observed in vascular cognitive impairment and vascular dementia, can be produced in

rats by clipping the common carotid arteries bilaterally. Since TNF-α is known to cause the degeneration of myelin, we examined whether these lesions can be ameliorated by ibudilast, a cAMP phosphodiesterase (PDE) inhibitor that suppresses tumor necrosis factor (TNF)-α production. After the ligation of both common carotid arteries in 29 rats, 21 rats received a daily oral administration of 10, 30 or 60 mg/kg ibudilast and 8 rats received vehicle for 14 days. The pathol. changes in the white matter were quantified in terms of white matter lesions and the emergence of activated microglia immunoreactive for major histocompatibility complex (MHC) antigen. In the vehicle-treated animals, white matter lesions and microglial activation occurred in the optic tract, internal capsule and corpus callosum. A low dose (10 mg/kg) of ibudilast failed to suppress the white matter lesions and microglial activation, whereas a dose of either 30 or 60 mg/kg ibudilast ameliorated these lesions ($p<0.001$). Without an alterations in laboratory blood data, 60 mg/kg ibudilast exhibited percent reduction of the white matter lesions ranging between 50% and 70%, which was more effective than 30 mg/kg ibudilast ($p<0.05$). The TNF-α immunoreactive glia decreased in number in the 60 mg/kg ibudilast-treated group as compared to the vehicle-treated group ($p<0.001$). These results indicate a dose-dependent protective effect of ibudilast against cerebrovascular white matter lesions and suggest a potential use for ibudilast in the treatment of vascular dementia.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ibudilast, a phosphodiesterase inhibitor, protects against white matter damage under chronic cerebral hypoperfusion in rat)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2003:296061 CAPLUS
DOCUMENT NUMBER:	138:297701
TITLE:	Transmucosal administration of phosphodiesterase inhibitors for the treatment of erectile dysfunction
INVENTOR(S):	Doherty, Paul C., Jr.; Place, Virgil A.; Smith, William L.
PATENT ASSIGNEE(S):	Vivus, Inc., USA
SOURCE:	U.S., 13 pp., Cont.-in-part of U.S. 6,037,346. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

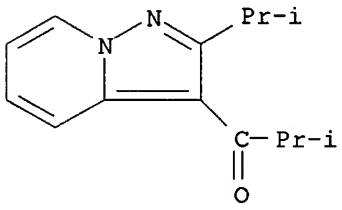
US 6548490	B1	20030415	US 1999-467094	19991210
US 6037346	A	20000314	US 1998-181070	19981027
CA 2394060	A1	20010614	CA 2000-2394060	20001208
WO 2001041807	A2	20010614	WO 2000-US33372	20001208
WO 2001041807	A3	20020214		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 200122566	A	20010618	AU 2001-22566	20001208
EP 1237577	A2	20020911	EP 2000-986297	20001208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003516363	T	20030513	JP 2001-543151	20001208
US 2002037828	A1	20020328	US 2001-888250	20010621
US 6403597	B2	20020611		
US 2002004498	A1	20020110	US 2001-938417	20010823
US 2003134861	A1	20030717	US 2003-351198	20030124
AU 2005248938	A1	20060202	AU 2005-248938	20051223
PRIORITY APPLN. INFO.:			US 1997-958816 B2	19971028
			US 1998-181070 A2	19981027
			US 1999-467094 A	19991210
			AU 2001-22566 A3	20001208
			WO 2000-US33372 W	20001208

AB A method is provided for treating erectile dysfunction in a mammalian male individual. The method involves the transmucosal administration of a phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or derivative thereof, within the context of an effective dosing regimen. Preferred modes of administration include transbuccal, sublingual and transrectal routes. Pharmaceutical formulations and kits are provided as well.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transmucosal administration of phosphodiesterase inhibitors for the treatment of erectile dysfunction)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:148544 CAPLUS
DOCUMENT NUMBER: 139:22169
TITLE: Enantioselective synthesis of a chiral pyridazinone

derivative by lipase-catalyzed hydrolysis

AUTHOR(S): Yoshida, Noriyuki; Aono, Masahiro; Tsubuki, Takeshi; Awano, Katsuya; Kobayashi, Tomoshige

CORPORATE SOURCE: Kyorin Pharmaceutical Co., Ltd., 2-5 Kandasurugadai, Chiyodaku, Tokyo, 101-8311, Japan

SOURCE: Tetrahedron: Asymmetry (2003), 14(5), 529-535
CODEN: TASYE3; ISSN: 0957-4166

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

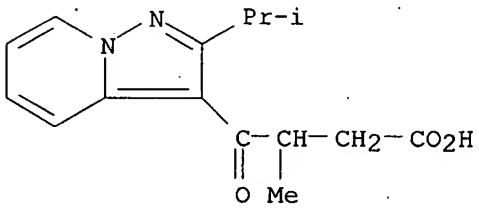
LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:22169

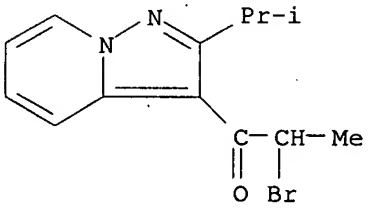
AB The lipase-catalyzed resolution of 2-(acyloxymethyl)-4,5-dihydro-5-methylpyridazin-3(2H)-one derivs. in organic solvents containing water was demonstrated to be a practical method for the synthesis of a chiral pyridazinone bearing a pyrazolopyridine ring, which is a potent phosphodiesterase inhibitor.

IT 204504-39-2P 204504-63-2P 537695-16-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(lipase-catalyzed hydrolytic resolution of 2-(acyloxymethyl)-4,5-dihydro-5-methylpyridazin-3(2H)-one derivs.)

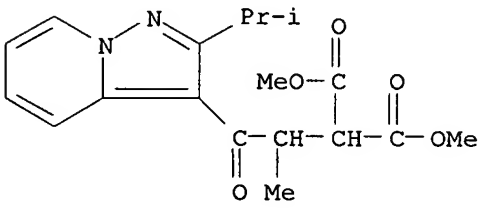
RN 204504-39-2 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, β-methyl-2-(1-methylethyl)-γ-oxo- (9CI) (CA INDEX NAME)



RN 204504-63-2 CAPLUS
CN 1-Propanone, 2-bromo-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 537695-16-2 CAPLUS
CN Propanedioic acid, [1-methyl-2-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-2-oxoethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



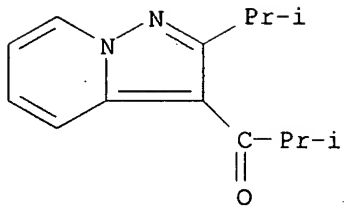
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:584018 CAPLUS
DOCUMENT NUMBER: 138:248260
TITLE: Relaxation and potentiation of cGMP-mediated response by ibudilast in bovine tracheal smooth muscle
AUTHOR(S): Nakahara, Tsutomu; Yunoki, Motonari; Moriuchi, Hiroshi; Mitani, Akiko; Sakamoto, Kenji; Ishii, Kunio
CORPORATE SOURCE: Department of Molecular Pharmacology, Kitasato University School of Pharmaceutical Sciences, Minato-ku, Tokyo, 108-8641, Japan
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2002), 366(3), 262-269
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of ibudilast, an inhibitor of phosphodiesterases (PDEs), on tension, levels of guanosine 3',5'-cyclic monophosphate (cGMP) and adenosine 3',5'-cyclic monophosphate (cAMP) were investigated in bovine tracheal smooth muscle. The authors especially examined the combined effect of ibudilast with the cGMP-elevating agents on these parameters. Ibudilast was equipotent to attenuate the precontractions induced by both 0.3 μM methacholine and 40 mM K+. By contrast, the relaxant effects of sodium nitroprusside and salbutamol on 40 mM K+-contracted prepns. were smaller than those on 0.3 μM methacholine-contracted ones. Neither Nω-nitro-L-arginine (100 μM), an inhibitor of nitric oxide synthase, nor ODQ (1H-[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one; 5 μM), an inhibitor of soluble guanylyl cyclase, affected the ibudilast-induced relaxation. The relaxations induced by ibudilast and diltiazem on 40 mM K+-contracted prepns. were significantly attenuated when extracellular CaCl2 was increased from 2.54 to 10 mM. Ibudilast (10 μM), which caused only minor effect by itself, significantly shifted the concentration-response curves for the relaxant responses to sodium nitroprusside (SNP), atrial natriuretic peptide (ANP), and salbutamol to the left. On the other hand, ibudilast did not change the relaxant responses to diltiazem. Unlike ibudilast, diltiazem (3 μM) failed to affect the SNP- and salbutamol-induced relaxations. Ibudilast significantly increased basal levels of cGMP and cAMP. Furthermore, ibudilast enhanced SNP (0.3 μM)- and ANP (0.3 μM)-induced cGMP accumulation and salbutamol (10 nM)-induced cAMP accumulation. Zaprinast (10 μM), a type 5 PDE inhibitor, enhanced both relaxation and cGMP accumulation induced by SNP and ANP without changing salbutamol-induced responses. These findings suggest that blockade of voltage-gated Ca2+ channels is involved in the relaxing action of ibudilast in bovine tracheal smooth muscle. However, ibudilast potentiates relaxation responses to ANP and SNP by inhibition of PDE 5, not by blockade of Ca2+ channels. The enhancement of cGMP-mediated response may contribute to the therapeutic effects of ibudilast.

IT 50847-11-5, Ibudilast
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(relaxation and potentiation of cGMP-mediated response by ibudilast in tracheal smooth muscle)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:575737 CAPLUS
DOCUMENT NUMBER: 137:135500
TITLE: Methods of inducing ovulation by administering a non-polypeptide cAMP level modulator
INVENTOR(S): Palmer, Stephen; McKenna, Sean; Tepper, Mark; Eshkol, Aliza; MacNamee, Michael C.
PATENT ASSIGNEE(S): Applied Research Systems Holding N.V., USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. Ser. No. 928,268.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103106	A1	20020801	US 2001-14812	20011214
US 6953774	B2	20051011		
US 2002065324	A1	20020530	US 2001-928268	20010810
CA 2469939	A1	20030626	CA 2001-2469939	20011214
AU 2002217111	A1	20030630	AU 2002-217111	20011214
AU 2002217111	B2	20070531		
EP 1463493	A1	20041006	EP 2001-274987	20011214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001017198	A	20041026	BR 2001-17198	20011214
CN 1582146	A	20050216	CN 2001-823951	20011214
JP 2005516924	T	20050609	JP 2003-552277	20011214
US 2005148501	A1	20050707	US 2003-498639	20011214
US 2006003925	A1	20060105	US 2005-169183	20050628
US 7078236	B2	20060718		
US 2006293222	A1	20061228	US 2006-456033	20060706

PRIORITY APPLN. INFO.:		
US 2000-224962P	P	20000811
US 2001-928268	A2	20010810
US 2001-14812	A3	20011214
WO 2001-EP14730	W	20011214
US 2005-169183	A1	20050628

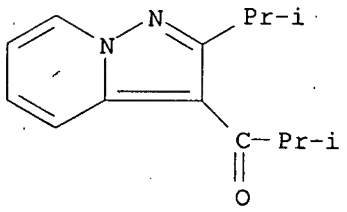
AB The present invention relates to methods of inducing ovulation in a female host comprising the administration of a non-polypeptide cAMP level modulator to the female host. In another aspect, the invention provides for specific administration of the phosphodiesterase inhibitor prior to the luteal phase of the host's ovulatory cycle. Preferred non-polypeptide cAMP level modulator include phosphodiesterase inhibitors, particularly inhibitors of phosphodiesterase 4 isoforms. Pharmaceutical compns. containing the cAMP modulators are also claimed.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods of inducing ovulation by administering a non-polypeptide cAMP level modulator)

RN 50847-11-5 CAPLUS .

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 25 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:334027 CAPLUS

DOCUMENT NUMBER: 137:379875

TITLE: Effect of phosphodiesterase inhibitors on nitric oxide production by glial cells

AUTHOR(S): Yoshikawa, Minka; Suzumura, Akio; Ito, Atsushi; Tamaru, Tsukasa; Takayanagi, Tetsuya

CORPORATE SOURCE: Department of Neurology, Nara Medical University, Nara, 634-0813, Japan

SOURCE: Tohoku Journal of Experimental Medicine (2002), 196(3), 167-177
CODEN: TJEMAO; ISSN: 0040-8727

PUBLISHER: Tohoku University Medical Press

DOCUMENT TYPE: Journal

LANGUAGE: English

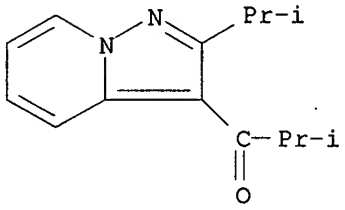
AB Nitric oxide (NO) is considered to play a crucial role in the development of various pathol. processes in the CNS, such as neuronal degeneration, inflammation and demyelination. In order to search for the agents which suppress NO production in the CNS, we examined the effects of one of the agents which elevate cAMP production, phosphodiesterase inhibitors (PDEIs), on NO production by glial cells in vitro. All the types of PDEIs, from type I- to V-specific and non-specific, suppressed the production of NO by mouse microglia and astrocytes stimulated with lipopolysaccharide, in a dose-dependent manner. Suppression of inducible NO synthase by PDEIs was confirmed by the expression of mRNA by RT-PCR. Although it required 10 μM or higher concentration to effectively suppress NO production in vitro, certain combinations of three different PDEIs synergistically suppressed NO production by astrocytes at 1 μM which could be obtained in vivo at usual therapeutic doses. Similarly, combinations of three PDEIs at 1 μM synergistically increased intracellular cAMP in astrocytes. The suppressive effects of PDEIs on NO production were abolished by addition of tumor necrosis factor α (TNFα). Thus, the main suppression mechanism of NO might be indirect through suppression of TNFα. Since some PDEIs are reported to pass through the blood-brain-barrier, the combination of three PDEIs may be worth trying in neurol. diseases, such as multiple sclerosis, human immunodeficiency virus-related neurol. diseases and other neurodegenerative disorders in which NO may play a crucial role.

IT 50847-11-5, Ibudilast
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effect of phosphodiesterase inhibitors on nitric oxide production by glial cells)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 26 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:241329 CAPLUS

DOCUMENT NUMBER: 136:284433

TITLE: Administration of phosphodiesterase inhibitors for the treatment of premature ejaculation

INVENTOR(S): Wilson, Leland F.; Doherty, Paul C.; Place, Virgil A.; Smith, William L.; Abdel-Hamid, Abdou Ali Ibrahim Aboubakr

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 467,094.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002037828	A1	20020328	US 2001-888250	20010621
US 6403597	B2	20020611		
US 6037346	A	20000314	US 1998-181070	19981027
US 6548490	B1	20030415	US 1999-467094	19991210
CA 2451152	A1	20030103	CA 2002-2451152	20020325
WO 2003000343	A2	20030103	WO 2002-US9415	20020325
WO 2003000343	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002248712	A1	20030108	AU 2002-248712	20020325
EP 1418896	A2	20040519	EP 2002-717729	20020325
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005519851	T	20050707	JP 2003-506984	20020325
AU 2005248938	A1	20060202	AU 2005-248938	20051223

PRIORITY APPLN. INFO.: US 1997-958816 B2 19971028

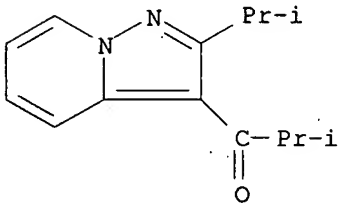
US 1998-181070	A2	19981027
US 1999-467094	A2	19991210
AU 2001-22566	A3	20001208
US 2001-888250	A	20010621
WO 2002-US9415	W	20020325

AB A method is provided for treatment of premature ejaculation by administration of a phosphodiesterase inhibitor, e.g., an inhibitor of a Type III, Type IV, or Type V phosphodiesterase. In a preferred embodiment, administration is on as "as needed" basis, i.e., the drug is administered immediately or several hours prior to sexual activity. Pharmaceutical formulations and packaged kits are also provided. Zaprinast 1.0, mannitol 1.0, microcryst. cellulose 2.0, and magnesium stearate 10 mg are blended in a suitable mixer and then compressed into sublingual tablets. Each sublingual tablet contains 10 mg zaprinast.

IT 50847-11-5, Ibudilast
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration of phosphodiesterase inhibitors for treatment of premature ejaculation)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 27 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:41645 CAPLUS
DOCUMENT NUMBER: 137:118839
TITLE: Ibudilast: a non-selective PDE inhibitor with multiple actions on blood cells and the vascular wall
AUTHOR(S): Kishi, Yukio; Ohta, Seiko; Kasuya, Natsuko; Sakita, Shinya; Ashikaga, Takashi; Isobe, Mitsuaki
CORPORATE SOURCE: Department of Cardiovascular Medicine, Tokyo Medical and Dental University, Tokyo, 113-8519, Japan
SOURCE: Cardiovascular Drug Reviews (2001), 19(3), 215-225
CODEN: CDREEA; ISSN: 0897-5957
PUBLISHER: Neva Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

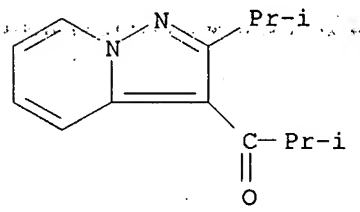
AB A review. Ibudilast (3-isobutyryl-2-isopropylpyrazolo[1,5-a]pyridine) is a nonselective inhibitor of cyclic nucleotide phosphodiesterase (PDE). It is widely used in Japan for improving prognosis and relieving symptoms in patients suffering from ischemic stroke or bronchial asthma. These clin. applications are based on the properties of ibudilast that inhibit platelet aggregation, improve cerebral blood flow and attenuate allergic reactions. The inhibition of platelet aggregation and vasodilatation by ibudilast may be due to synergistic elevation of intracellular cyclic nucleotides and release of nitric oxide (NO) or prostacyclin from endothelium, rather than direct inhibition of PDE5 or PDE3. Another important property of ibudilast is its antiinflammatory activity possibly associated with potent inhibition of PDE4. Combined with its relaxing effects on bronchial smooth muscle, antiinflammatory activity of ibudilast

could favorably influence pathophysiol. of asthma by antagonizing chemical mediators triggering asthmatic attacks. Ibudilast was also reported to significantly attenuate inflammatory cell infiltration in the lumbar spinal cord in an animal model of encephalomyelitis. Future investigations should include effects of ibudilast on inflammatory reactions between endothelium and blood cells, which may initiate the development of atherosclerosis.

IT 50847-11-5, Ibudilast
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ibudilast as a nonselective PDE inhibitor with multiple actions on blood cells and vascular wall)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 28 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:561569 CAPLUS

DOCUMENT NUMBER: 135:338959

TITLE: Ibudilast attenuates astrocyte apoptosis via cyclic GMP signalling pathway in an in vitro reperfusion model

AUTHOR(S): Takuma, K.; Lee, E.; Enomoto, R.; Mori, K.; Baba, A.; Matsuda, T.

CORPORATE SOURCE: Department of Analytical Chemistry, Kobe Gakuin University, Kobe, 651-2180, Japan

SOURCE: British Journal of Pharmacology (2001), 133(6), 841-848
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

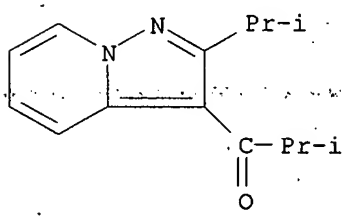
AB 1 We examined the effect of 3-isobutyryl-2-isopropylpyrazolo[1,5-a]pyridine (ibudilast), which has been clin. used for bronchial asthma and cerebrovascular disorders, on cell viability induced in a model of reperfusion injury. 2 Ibudilast at 10-100 μM significantly attenuated the H2O2-induced decrease in cell viability. 3 Ibudilast inhibited the H2O2-induced cytochrome c release, caspase-3 activation, DNA ladder formation and nuclear condensation, suggesting its anti-apoptotic effect. 4 Phosphodiesterase inhibitors such as theophylline, pentoxyfylline, vinpocetine, dipyridamole and zaprinast, which increased the guanosine-3',5'-cyclic monophosphate (cGMP) level, and dibutyryl cGMP attenuated the H2O2-induced injury in astrocytes. 5 Ibudilast increased the cGMP level in astrocytes. 6 The cGMP-dependent protein kinase inhibitor KT5823 blocked the protective effects of ibudilast and dipyridamole on the H2O2-induced decrease in cell viability, while the cAMP-dependent protein kinase inhibitor KT5720, the cAMP antagonist Rp-cyclic AMPS, the mitogen-activated protein/extracellular signal-regulated kinase inhibitor PD98059 and the leukotriene D4 antagonist LY 171883 did

not. 7 KT5823 also blocked the effect of ibudilast on the H2O2-induced cytochrome c release and caspase-3-like protease activation. 8 These findings suggest that ibudilast prevents the H2O2-induced delayed apoptosis of astrocytes via a cGMP, but not cAMP, signaling pathway.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ibudilast attenuates rat astrocyte apoptosis via a cyclic GMP, but not a cAMP, signaling pathway in an in vitro reperfusion model)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 29 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:434902 CAPLUS
DOCUMENT NUMBER: 135:51053
TITLE: Transmucosal administration of phosphodiesterase inhibitors for the treatment of erectile dysfunction
INVENTOR(S): Doherty, Paul C., Jr.; Place, Virgil A.; Smith, William L.
PATENT ASSIGNEE(S): Vivus, Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

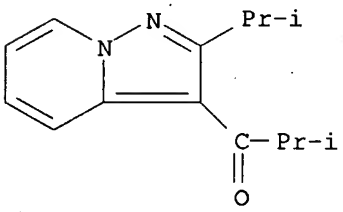
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001041807	A2	20010614	WO 2000-US33372	20001208
WO 2001041807	A3	20020214		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6548490	B1	20030415	US 1999-467094	19991210
CA 2394060	A1	20010614	CA 2000-2394060	20001208
AU 200122566	A	20010618	AU 2001-22566	20001208
EP 1237577	A2	20020911	EP 2000-986297	20001208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003516363	T	20030513	JP 2001-543151	20001208

AU 2005248938 A1 20060202 AU 2005-248938 20051223
PRIORITY APPLN. INFO.: US 1999-467094 A 19991210
US 1997-958816 B2 19971028
US 1998-181070 A2 19981027
AU 2001-22566 A3 20001208
WO 2000-US33372 W 20001208

AB A method is provided for treating erectile dysfunction in a mammalian male individual. The method involves the transmucosal administration of a phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or derivative thereof, within the context of an effective dosing regimen. Preferred modes of administration include transbuccal, sublingual and transrectal routes. Pharmaceutical formulations and kits are provided as well. Thus, a buccal dosage form was prepared from 10 g sildenafil citrate and 90 g gelatin. After the mixing was complete, 20 g concentrated glycerin, 10 g lactose and 20 g mannitol were added and the components were mixed until uniform. Aliquot portions (150 mg) of the mixture were compression-molded to provide a buccal dosage unit. Each buccal unit contained 10 mg sildenafil citrate.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transmucosal administration of phosphodiesterase inhibitors for treatment of erectile dysfunction)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 30 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:152520 CAPLUS
DOCUMENT NUMBER: 134:202703
TITLE: Synergistic combination of a phosphodiesterase (PDE) inhibitor and a β2-adrenoceptor agonist for treatment of respiratory tract disorders
INVENTOR(S): Beume, Rolf; Bundschuh, Daniela; Hatzelmann, Armin; Schudt, Christian; Weimar, Christian; Kilian, Ulrich
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001013953	A2	20010301	WO 2000-EP7852	20000811
WO 2001013953	A3	20010920		

W: AE, AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE

CA 2381802	A1	20010301	CA 2000-2381802	20000811
BR 2000013478	A	20020430	BR 2000-13478	20000811
EP 1212089	A2	20020612	EP 2000-954625	20000811
EP 1212089	B1	20060322		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
TR 200201317	T2	20021121	TR 2002-1317	20000811
HU 200203098	A2	20030128	HU 2002-3098	20000811
JP 2003507435	T	20030225	JP 2001-518088	20000811
NZ 517166	A	20040130	NZ 2000-517166	20000811
AU 777012	B2	20040930	AU 2000-67016	20000811
AT 320800	T	20060415	AT 2000-954625	20000811
EP 1671651	A1	20060621	EP 2006-110822	20000811
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PT 1212089	T	20060831	PT 2000-954625	20000811
ES 2260043	T3	20061101	ES 2000-954625	20000811
IN 2002MN00066	A	20050218	IN 2002-MN66	20020118
NO 2002000815	A	20020219	NO 2002-815	20020219
ZA 2002001389	A	20020821	ZA 2002-1389	20020219
US 6624181	B1	20030923	US 2002-49999	20020220
MX 2002PA01830	A	20020812	MX 2002-PA1830	20020221
HK 1047244	A1	20061027	HK 2002-108936	20021209
US 2004034087	A1	20040219	US 2003-437005	20030514
US 7056936	B2	20060606		
US 2006079539	A1	20060413	US 2005-286391	20051125
US 2006205806	A1	20060914	US 2006-433419	20060515

PRIORITY APPLN. INFO.:

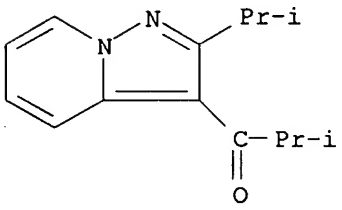
EP 1999-116447	A	19990821
DE 1997-19708049	A	19970228
WO 1998-EP1047	W	19980224
US 1999-367850	A2	19990827
EP 2000-954625	A3	20000811
WO 2000-EP7852	W	20000811
US 2002-49999	A1	20020220
US 2003-437005	A1	20030514
US 2005-286391	A1	20051125

AB The invention discloses the combined administration of PDE inhibitors and β2-adrenoceptor agonists for the treatment of respiratory tract disorders.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase inhibitor-β2-adrenoceptor agonist synergistic combination for treatment of respiratory tract disorders)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 31 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:855762 CAPLUS
DOCUMENT NUMBER: 134:25367
TITLE: Local administration of Type III phosphodiesterase inhibitors for the treatment of erectile dysfunction
INVENTOR(S): Doherty, Paul C., Jr.; Place, Virgil A.; Smith, William L.
PATENT ASSIGNEE(S): Vivus, Inc., USA
SOURCE: U.S., 16 pp., Cont.-in-part of U.S. 6,037,346.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6156753	A	20001205	US 1999-437682	19991110
US 6037346	A	20000314	US 1998-181070	19981027
AU 2005248938	A1	20060202	AU 2005-248938	20051223

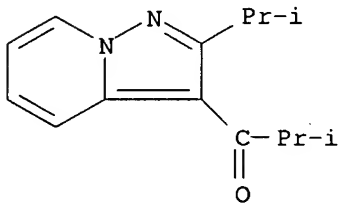
PRIORITY APPLN. INFO.:

US 1997-958816	B2	19971028
US 1998-181070	A2	19981027
AU 2001-22566	A3	20001208

AB A method is provided for treating erectile dysfunction, e.g., vasculogenic erectile dysfunction such as vasculogenic impotence. The method involves the administration of a Type III phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or derivative thereof, wherein administration is transurethral, topical or transdermal. A preferred mode of administration is transurethral. Pharmaceutical formulations and kits are provided as well.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase III inhibitor local administration for treatment of erectile dysfunction)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



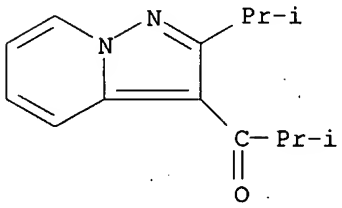
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 32 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:458686 CAPLUS
DOCUMENT NUMBER: 133:159758
TITLE: Ibudilast modulates platelet-endothelium interaction mainly through cyclic GMP-dependent mechanism
AUTHOR(S): Kishi, Yukio; Ohta, Seiko; Kasuya, Natsuko; Tatsumi, Masahiro; Sawada, Mitsunori; Sakita, Shinya; Ashikaga, Takashi; Numano, Fujio
CORPORATE SOURCE: Department of Cardiology, Tokyo Medical and Dental University, Tokyo, 113-8519, Japan

SOURCE: Journal of Cardiovascular Pharmacology (2000), 36(1), 65-70
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 3-Isobutyryl-2-isopropylpyrazolo[1,5-a]pyridine (ibudilast) has been widely used in Japanese clinics for its antiasthmatic and antithrombotic effects. We investigated the mechanisms involved in the antiplatelet effects of the agent, specifically focusing on platelet-endothelium interaction. Ibudilast inhibits both phosphodiesterase (PDE) 3 and 5, the two major PDE isoforms of human platelets, with an IC50 of 31 and 2.2 μM, resp. Cyclic guanosine monophosphate (GMP) accumulation in washed human platelets exposed to ibudilast alone increased significantly only at high concns. of the agent (100 μM), whereas ≥ 1 μM ibudilast enhanced cGMP levels in the platelets cocultured with bovine aorta endothelial cells (ECs). In contrast, ibudilast enhanced cAMP accumulation only at 100 μM, either with or without ECs. The synergistic effect of ibudilast and EC on cyclic nucleotide accumulation also was demonstrated by the inhibitory capability of the drug and the cells on platelet aggregation. The synergism between ibudilast and aspirin-pretreated ECs was more pronounced than that between ibudilast and Nω-nitro-L-arginine (L-NNA)-pretreated ECs. Ibudilast affected neither ATP diphosphohydrolase activity nor NO release from EC up to a concentration of 10 μM. We conclude that ibudilast exhibits antiplatelet properties mainly by inhibiting PDE5 to potentiate antiplatelet function of endothelium-derived NO.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ibudilast modulates platelet-endothelium interaction mainly through cyclic GMP-dependent mechanism)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

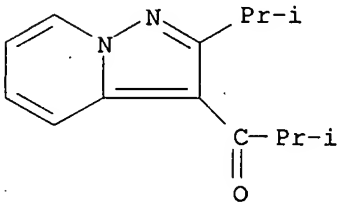
L7 ANSWER 33 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:574766 CAPLUS
DOCUMENT NUMBER: 131:281462
TITLE: Ibudilast suppresses TNFα production by glial cells functioning mainly as type III phosphodiesterase inhibitor in the CNS
AUTHOR(S): Suzumura, Akio; Ito, Atsushi; Yoshikawa, Minka; Sawada, Makoto
CORPORATE SOURCE: Department of Neurology, Nara Medical University, Nara, 634-0813, Japan
SOURCE: Brain Research (1999), 837(1,2), 203-212

CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tumor necrosis factor α (TNFα) is considered to play a critical role in the development of various pathol. processes in the central nervous system (CNS), such as neuronal degeneration, demyelination and HIV-related pathol. To search for the agents which suppress TNFα production in the CNS for future treatment of these pathol. conditions, we examined the effects of ibudilast on TNFα production by murine microglia and astrocytes. Some actions of ibudilast are reportedly mediated by inhibition of type IV phosphodiesterase (PDE). Type IV PDE inhibitor has been shown to be the most effective for exptl. autoimmune inflammatory demyelination. Therefore, we also determined the subtype of PDE inhibited by ibudilast. Ibudilast significantly and selectively suppressed TNFα production by microglia in a dose-dependent manner, without affecting their viability. The inhibition assay indicated that ibudilast is a rather selective inhibitor for type III PDE purified from brain, heart and kidney with moderate inhibitory activity against types I, II and IV PDEs from various tissues. Although it required 10 μM or higher concns. to effectively suppress TNFα production in vitro, the combination of ibudilast with other subtypes of PDE inhibitors synergistically suppressed TNFα and nitric oxide production by microglia at 1 μM, a similar concentration that could be obtained in vivo at usual therapeutic dose. Thus, ibudilast, when used in a combination with other PDE inhibitors, will be useful for future strategies to treat intractable neurol. diseases in which TNFα may play a causative role.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic effects of ibudilast and phosphodiesterase inhibitors on glial cell TNFα production)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

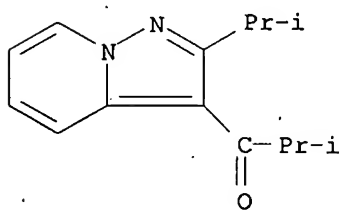
L7 ANSWER 34 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:536656 CAPLUS
DOCUMENT NUMBER: 131:295264
TITLE: Suppression of anti-CD3-induced interleukin-4 and interleukin-5 release from splenocytes of Mesocestoides corti-infected BALB/c mice by phosphodiesterase 4 inhibitors
AUTHOR(S): Souness, John E.; Houghton, Clare; Sardar, Nughat; Withnall, Michael T.
CORPORATE SOURCE: Rhone-Poulenc Rorer Central Research, Dagenham Research Centre, Essex, RM10 7XS, UK

SOURCE: Biochemical Pharmacology (1999), 58(6), 991-999
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We investigated the suppressive effects of rolipram, RP 73401 (piclamilast), and other structurally diverse inhibitors of adenosine 3'5'-cyclic monophosphate (cAMP)-specific phosphodiesterase (PDE4) on anti-CD3-stimulated interleukin (IL)-4 and IL-5 generation by splenocytes from BALB/c mice infected with Mesocestoides (M) corti. RP 73401 (IC40: 0.011 ± 0.004 μM) was a very potent inhibitor of anti-CD3-induced IL-4 release, being apprx.40-fold more potent than (±)-rolipram (IC40: 0.43 ± 0.09 μM). A maximal inhibition of 60-70% of the response was achieved at the top concns. of RP 73401 (1 μM) and rolipram (100 μM). These PDE inhibitors also suppressed IL-5 generation over the same concentration ranges, but the maximal suppression achieved was only 30-40%. R-(−)-rolipram (IC40: 0.39 ± 0.09 μM) was apprx.6-fold more potent than S-(+)- rolipram (IC40: 2.6 ± 0.95 μM) in inhibiting IL-4 release. A close correlation (r2 = 0.82) was observed between suppression of IL-4 release by PDE inhibitors and inhibition of CTLL cell PDE4, a form against which R-(-)-rolipram displayed relatively weak inhibitory potency. A poorer correlation (r2 = 0.26) was observed between suppression of IL-4 release and affinities of cAMP PDE inhibitors for the high-affinity rolipram binding site in mouse brain membranes. The cGMP-inhibited PDE (PDE3) inhibitor, siguazodan, had little or no effect (IC40 > 100 μM) on anti-CD3-stimulated release of either IL-4 or IL-5 and did not significantly enhance the inhibitory action of RP 73401 on the release of either of these cytokines. Finally, RP 73401 (IC50: 0.41 ± 0.19 nM) inhibited anti-CD3-stimulated DNA synthesis in splenocyte prepns. from M. corti-infected mice and siguazodan (10 μM) had no effect on this response, either alone or in combination with the PDE4 inhibitor. The results show that PDE4 inhibitors suppress the release of Th2 cytokines from anti-CD3-stimulated murine spenocytes and that this effect is correlated with inhibition of a low-affinity PDE4 form.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 inhibitors suppression of anti-CD3-induced IL-4 and IL-5 release from splenocytes of Mesocestoides corti infection)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



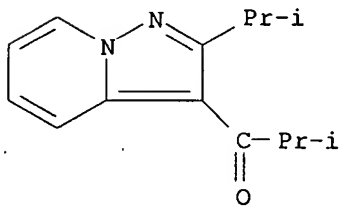
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 35 OF 44 CAPLUS

ACCESSION NUMBER: 1999:113052 CAPLUS
DOCUMENT NUMBER: 131:39382
TITLE: Ibudilast, a phosphodiesterase inhibitor, ameliorates experimental autoimmune encephalomyelitis in Dark August rats
AUTHOR(S): Fujimoto, Tetsuo; Sakoda, Saburo; Fujimura, Harutoshi; Yanagihara, Takehiko
CORPORATE SOURCE: Department of Neurology, Osaka University Medical School, Suita, Osaka, 565-0871, Japan
SOURCE: Journal of Neuroimmunology (1999), 95(1,2), 35-42
CODEN: JNRIDW; ISSN: 0165-5728
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A phosphodiesterase inhibitor (PDEI), Ibudilast, which has been in wide use for the management of bronchial asthma and cerebrovascular disease in Japan, was tested for its clin. efficacy on exptl. autoimmune encephalomyelitis (EAE) in Dark August rats. The severity of acute EAE was significantly ameliorated by prophylactic oral treatment with Ibudilast (10 mg/kg per day) starting on the day of immunization, although it did not modify the course of the disease when it was given after the onset of the first clin. sign of EAE. Histol., inflammatory cell infiltration in the lumbar spinal cord was significantly reduced in Ibudilast-treated animals as compared to control animals. Ibudilast mildly suppressed MBP-induced proliferation of T cells in regional lymph nodes, the secretion of interferon-γ from T cells activated by MBP in CFA, and the secretion of tumor necrosis factor-α from macrophages. While the in vitro studies did not suggest difference between Ibudilast and other PDEIs such as rolipram, the clin. dose of Ibudilast is .apprx.200-fold higher than that of rolipram and the ED of Ibudilast was relatively close to what has been therapeutically used in patients. Thus, Ibudilast may be a candidate for clin. use for patients with multiple sclerosis.

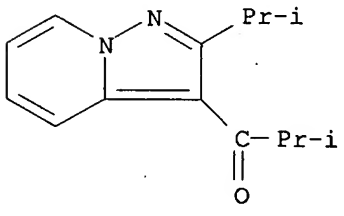
IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase inhibitor ibudilast ameliorates autoimmune encephalomyelitis: relevance for multiple sclerosis treatment)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 36 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:344010 CAPLUS
DOCUMENT NUMBER: 129:76860
TITLE: Cyclic AMP-elevating agents prevent oligodendroglial excitotoxicity
AUTHOR(S): Yoshioka, Akira; Shimizu, Yuko; Hirose, Genjiro;

Kitasato, Hiroshi; Pleasure, David
CORPORATE SOURCE: Department of Neurology, Kanazawa Medical University, Ishikawa, Japan
SOURCE: Journal of Neurochemistry (1998), 70(6), 2416-2423
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previously, the authors have demonstrated that cells of the oligodendroglial lineage express non-NMDA glutamate receptor genes and are damaged by kainate-induced Ca2+ influx via non-NMDA glutamate receptor channels, representing oligodendroglial excitotoxicity. The authors find in the present study that agents that elevate intracellular cAMP prevent oligodendroglial excitotoxicity. After oligodendrocyte-like cells, differentiated from the CG-4 cell line established from rat oligodendrocyte type-2 astrocyte progenitor cells, were exposed to 2 mM kainate for 24 h, cell death was evaluated by measuring activity of lactate dehydrogenase released into the culture medium. Released lactate dehydrogenase increased about 3-fold when exposed to 2 mM kainate. Kainate-induced cell death was prevented by the following agents: adenylate cyclase activator (forskolin), cAMP analogs (dibutyryl cAMP and 8-bromo-cAMP), and cAMP phosphodiesterase inhibitors (3-isobutyl-1-methylxanthine, pentoxifylline, propentofylline, and ibudilast). Simultaneous addition of both forskolin and phosphodiesterase inhibitors prevented the kainate-induced cell death in an additive manner. A remarkable increase in Ca2+ influx (.apprx.5.5-fold) also was induced by kainate. The cAMP-elevating agents caused a partial suppression of the kainate-induced increase in Ca2+ influx, leading to a less prominent response of intracellular Ca2+ concentration to kainate. The suppressing effect of forskolin on the kainate-induced Ca2+ influx was partially reversed by H-89, an inhibitor of cAMP-dependent protein kinase. In contrast to this, okadaic acid, an inhibitor of protein phosphatases 1 and 2A, brought about a decrease in the kainate-induced Ca2+ influx. The authors therefore concluded that cAMP-elevating agents prevented oligodendroglial excitotoxicity by cAMP-dependent protein kinase-dependent protein phosphorylation, resulting in decreased kainate-induced Ca2+ influx.
IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cAMP-elevating agents prevent kainate-induced oligodendroglial excitotoxicity)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 37 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:219808 CAPLUS
DOCUMENT NUMBER: 128:230381

TITLE: Preparation of pyrazolopyridylpyridazinone derivatives as phosphodiesterase inhibitors

INVENTOR(S): Kouno, Yasushi; Ogata, Takenobu; Awano, Katsuya; Matsuzawa, Kayoko; Tooru, Taroh

PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9814448	A1	19980409	WO 1997-JP3434	19970926
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2267103	A1	19980409	CA 1997-2267103	19970926
CA 2267103	C	20060530		
AU 9743213	A	19980424	AU 1997-43213	19970926
AU 733316	B2	20010510		
CN 1232463	A	19991020	CN 1997-198468	19970926
CN 1083841	B	20020501		
HU 9903018	A2	20000328	HU 1999-3018	19970926
EP 989129	A1	20000329	EP 1997-941255	19970926
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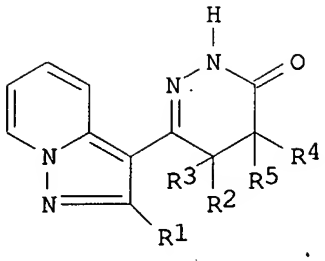
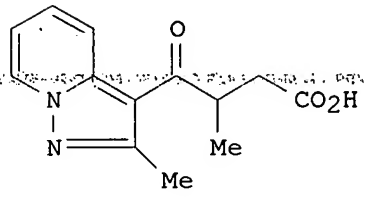
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 229527	T	20021215	AT 1997-941255	19970926
ES 2187814	T3	20030616	ES 1997-941255	19970926
TW 494100	B	20020711	TW 1997-86114443	19971003
KR 2000048874	A	20000725	KR 1999-702884	19990402
US 6265577	B1	20010724	US 1999-269734	19990405
PRIORITY APPLN. INFO.:			JP 1996-283148 A	19961004
			WO 1997-JP3434 W	19970926

OTHER SOURCE(S): MARPAT 128:230381

GI



I

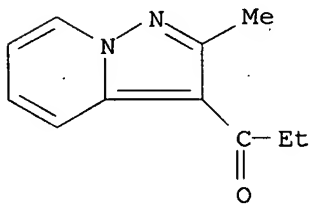


II

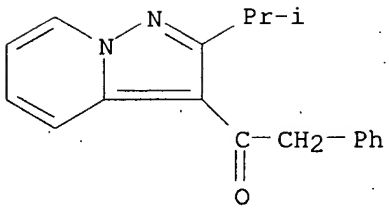
AB Novel pyrazolopyridylpyridazinone derivs. (I; R1 = C1-4 alkyl or C3-6 cycloalkyl; R2-R5 = H, C1-4 alkyl, Ph, or alternatively R3 and R5 may be united to form a double bond) are prepared I possess phosphodiesterase inhibiting activity and have a selective potent bronchodilating effect on the respiratory tract. Thus, compound (II; preparation given) was refluxed with NH2NH2.H2O in EtOH to give I (R1 = R2 = Me, R3-R5 = H). One of I was tested and showed bronchodilating effect on the respiratory tract.

IT 151831-27-5 204504-62-1 204504-63-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrazolopyridylpyridazinone derivs. as phosphodiesterase inhibitors)

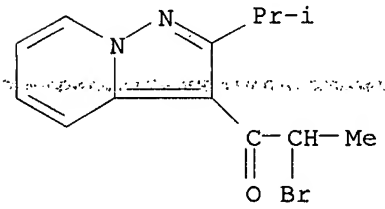
RN 151831-27-5 CAPLUS
CN 1-Propanone, 1-(2-methylpyrazolo[1,5-a]pyridin-3-yl)- (9CI) (CA INDEX NAME)



RN 204504-62-1 CAPLUS
CN Ethanone, 1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-2-phenyl- (9CI) (CA INDEX NAME)



RN 204504-63-2 CAPLUS
CN 1-Propanone, 2-bromo-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-(9CI) (CA INDEX NAME)



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204504-28-9P 204504-29-0P 204504-30-3P
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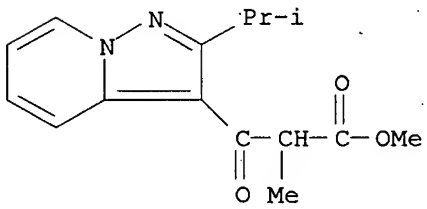
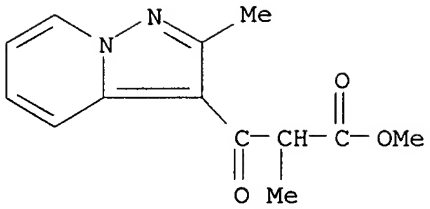
204504-38-1P 204504-39-2P 204504-40-5P
204504-42-7P 204504-43-8P 204504-44-9P
204504-45-0P 204504-46-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrazolopyridylpyridazinone derivs. as phosphodiesterase inhibitors)

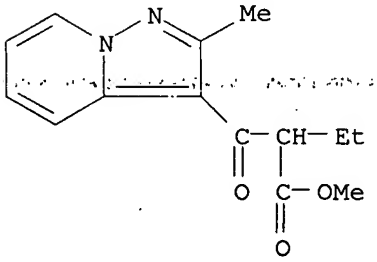
RN 141418-12-4 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-propanoic acid, α-methyl-2-(1-methylethyl)-β-oxo-, methyl ester (9CI) (CA INDEX NAME)



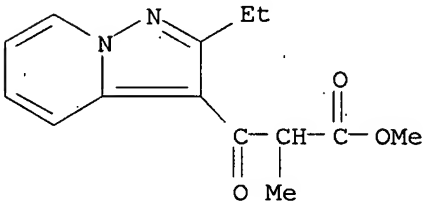
RN 204504-19-8 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-propanoic acid, α,2-dimethyl-β-oxo-, methyl ester (9CI) (CA INDEX NAME)



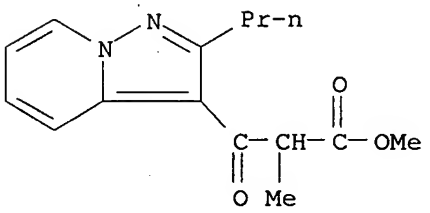
RN 204504-20-1 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-propanoic acid, α-ethyl-2-methyl-β-oxo-, methyl ester (9CI) (CA INDEX NAME)



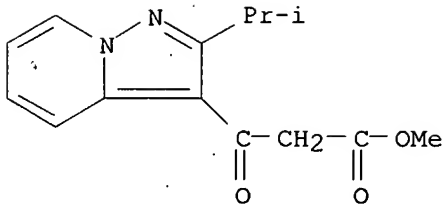
RN 204504-21-2 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-propanoic acid, 2-ethyl-α-methyl-β-oxo-, methyl ester (9CI) (CA INDEX NAME)



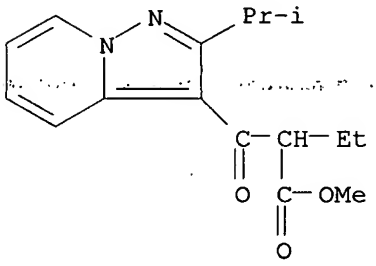
RN 204504-22-3 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-propanoic acid, α-methyl-β-oxo-2-propyl-, methyl ester (9CI) (CA INDEX NAME)



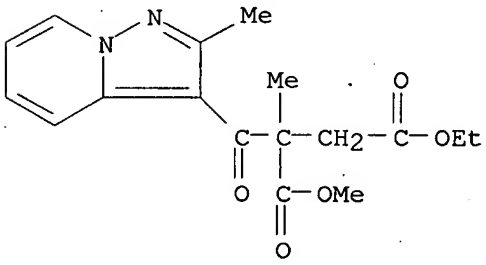
RN 204504-23-4 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-propanoic acid, 2-(1-methylethyl)-β-oxo-, methyl ester (9CI) (CA INDEX NAME)



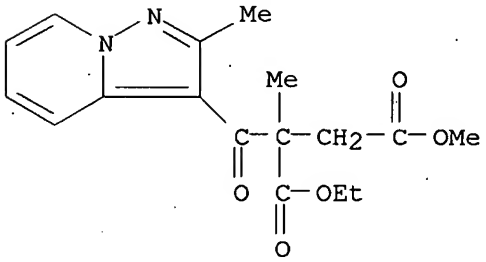
RN 204504-24-5 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-propanoic acid, α-ethyl-2-(1-methylethyl)-β-oxo-, methyl ester (9CI) (CA INDEX NAME)



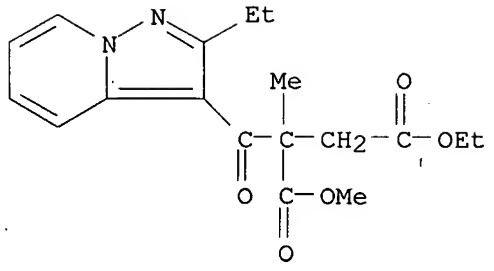
RN 204504-26-7 CAPLUS
CN Butanedioic acid, 2-methyl-2-[(2-methylpyrazolo[1,5-a]pyridin-3-yl)carbonyl]-, 4-ethyl 1-methyl ester (9CI) (CA INDEX NAME)



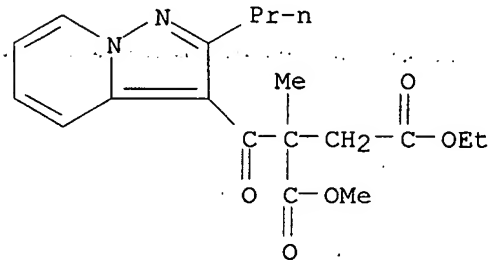
RN 204504-27-8 CAPLUS
CN Butanedioic acid, 2-methyl-2-[(2-methylpyrazolo[1,5-a]pyridin-3-yl)carbonyl]-, 1-ethyl 4-methyl ester (9CI) (CA INDEX NAME)



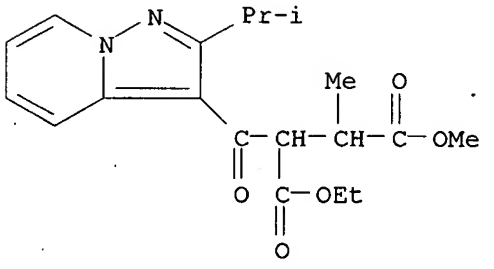
RN 204504-28-9 CAPLUS
CN Butanedioic acid, 2-[(2-ethylpyrazolo[1,5-a]pyridin-3-yl)carbonyl]-2-methyl-, 4-ethyl 1-methyl ester (9CI) (CA INDEX NAME)



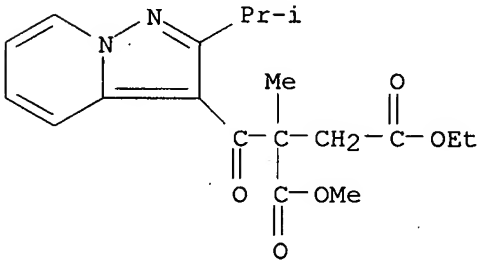
RN 204504-29-0 CAPLUS
CN Butanedioic acid, 2-methyl-2-[(2-propylpyrazolo[1,5-a]pyridin-3-yl)carbonyl]-, 4-ethyl 1-methyl ester (9CI) (CA INDEX NAME)



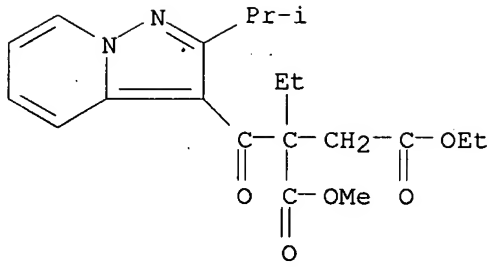
RN 204504-30-3 CAPLUS
CN Butanedioic acid, 2-methyl-3-[[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]carbonyl]-, 4-ethyl 1-methyl ester (9CI) (CA INDEX NAME)



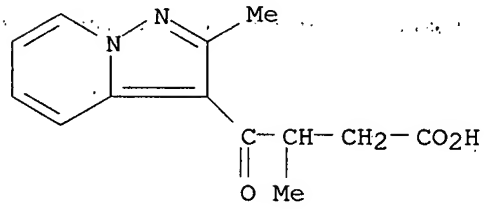
RN 204504-31-4 CAPLUS
CN Butanedioic acid, 2-methyl-2-[[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]carbonyl]-, 4-ethyl 1-methyl ester (9CI) (CA INDEX NAME)



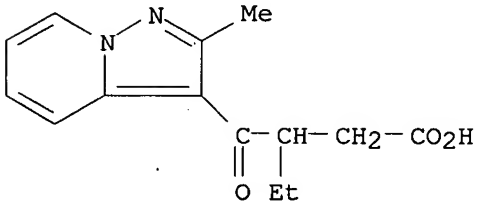
RN 204504-32-5 CAPLUS
CN Butanedioic acid, 2-ethyl-2-[[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]carbonyl]-, 4-ethyl 1-methyl ester (9CI) (CA INDEX NAME)



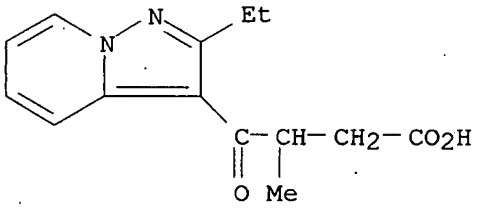
RN 204504-34-7 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, β,2-dimethyl-γ-oxo- (9CI) (CA INDEX NAME)



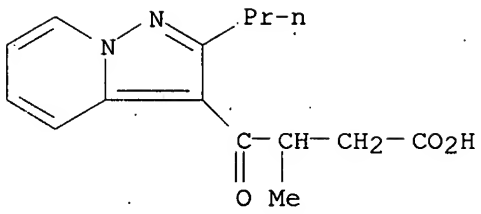
RN 204504-35-8 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, β-ethyl-2-methyl-γ-oxo- (9CI) (CA INDEX NAME)



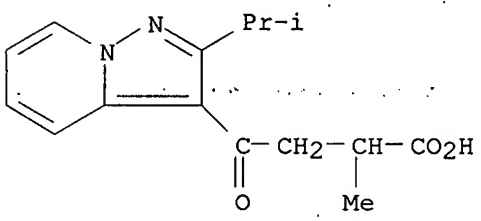
RN 204504-36-9 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, 2-ethyl-β-methyl-γ-oxo- (9CI) (CA INDEX NAME)



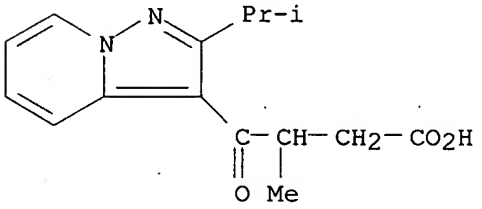
RN 204504-37-0 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, β-methyl-γ-oxo-2-propyl- (9CI) (CA INDEX NAME)



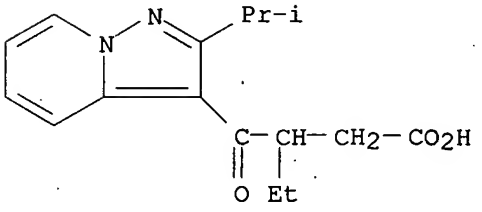
RN 204504-38-1 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, α-methyl-2-(1-methylethyl)-γ-oxo- (9CI) (CA INDEX NAME)



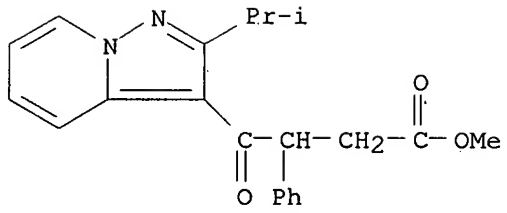
RN 204504-39-2 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, β-methyl-2-(1-methylethyl)-γ-oxo- (9CI) (CA INDEX NAME)



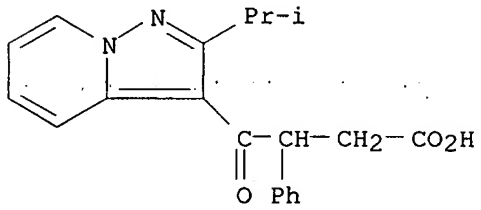
RN 204504-40-5 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, β-ethyl-2-(1-methylethyl)-γ-oxo- (9CI) (CA INDEX NAME)



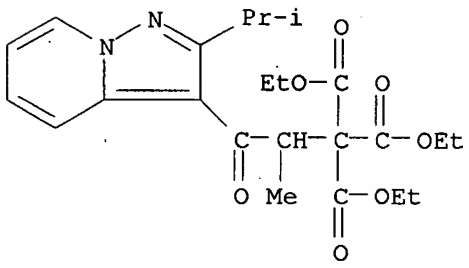
RN 204504-42-7 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, 2-(1-methylethyl)-γ-oxo-β-phenyl-, methyl ester (9CI) (CA INDEX NAME)



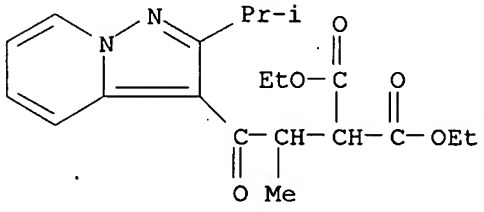
RN 204504-43-8 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, 2-(1-methylethyl)-γ-oxo-β-phenyl- (9CI) (CA INDEX NAME)



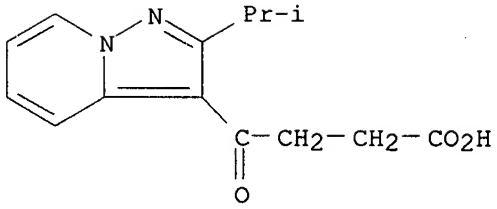
RN 204504-44-9 CAPLUS
CN 1,1,1-Propanetricarboxylic acid, 2-methyl-3-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-3-oxo-, triethyl ester (9CI) (CA INDEX NAME)



RN 204504-45-0 CAPLUS
CN Propanedioic acid, [1-methyl-2-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-2-oxoethyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 204504-46-1 CAPLUS
CN Pyrazolo[1,5-a]pyridine-3-butanoic acid, 2-(1-methylethyl)-γ-oxo- (9CI) (CA INDEX NAME)

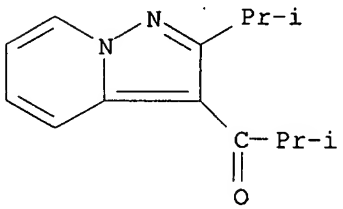


REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 38 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:127313 CAPLUS
DOCUMENT NUMBER: 128:176034
TITLE: Inhibitory effect of ibudilast (KC-404) on cyclic nucleotide phosphodiesterases
AUTHOR(S): Murashima, Seiko; Nagami, Keiko; Kawahara, Noriko; Sugiasaki, Hitomi
CORPORATE SOURCE: Mie Prefectural College of Nursing, Tsu, 514-0116, Japan
SOURCE: Yakuri to Chiryo (1998), 26(1), 41-45
CODEN: YACHDS; ISSN: 0386-3603
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Inhibitory effects of ibudilast on the phosphodiesterase (PDE) isoenzymes were investigated in vitro. Ibudilast weakly inhibited activities of PDE III and PDE V isolated from human platelets at IC50 values of 50 and 5.2 μM, resp. On the other hand, ibudilast remarkably inhibited both PDE II and PDE IV obtained from cultured human umbilical cord vein endothelial cells (HUVEC) at IC50 values of less than 0.1 μM. Ibudilast also revealed strong inhibition on bovine brain PDE IV activity comparable to that of rolipram, an IC50 value being 0.65 μM. The results suggest that ibudilast is a selective PDE inhibitor for type II and IV PDE isoenzymes.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitory effect of ibudilast (KC-404) on cyclic nucleotide phosphodiesterases)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 39 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:419635 CAPLUS
DOCUMENT NUMBER: 127:130621
TITLE: Evidence that cyclic AMP phosphodiesterase inhibitors suppress interleukin-2 release from

murine splenocytes by interacting with a "low-affinity" phosphodiesterase 4 conformer

AUTHOR(S): Souness, John E.; Houghton, Clare; Sardar, Nughat; Withnall, Michael T.

CORPORATE SOURCE: Rhone-Poulenc Rorer Central Research, Dagenham Research Center, Essex, RM10 7XS, UK

SOURCE: British Journal of Pharmacology (1997), 121(4), 743-750
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Stockton

DOCUMENT TYPE: Journal

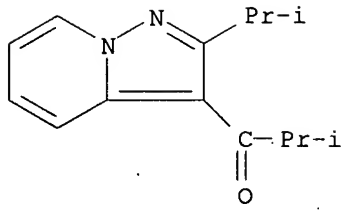
LANGUAGE: English

AB The authors have investigated the suppressive effects of rolipram, RP 73401 (piclamilast) and other structurally diverse inhibitors of cAMP-specific phosphodiesterase 4 (PDE4) on interleukin (IL)-2 generation from Balb/c mouse splenocytes exposed to the superantigen, Staphylococcal enterotoxin-A (Staph. A). The purpose was to determine whether their potencies are more closely correlated with inhibition of PDE4 from CTLL cells, against which rolipram displays weak potency (low-affinity PDE4), or displacement of [3H]-(±)-rolipram from its high-affinity binding site (HARBS) in mouse brain cytosol. RP 73401 (IC50 0.46 nM) was a very potent inhibitor of Staph. A-induced IL-2 release from Balb/c mouse splenocytes, being > 1100 fold more potent than ()-rolipram (IC 540 nM). A close correlation (r=0.95) was observed between suppression of IL-2 release by PDE inhibitors and inhibition of PDE4. In contrast, little correlation (r=0.39) was observed between suppression of IL-2 release and their affinities for the high-affinity rolipram binding site (HARBS). RP 73401 only inhibited partially (30-40%) Staph. A-induced incorporation of [H]-thymidine into splenocyte DNA. The PDE3 inhibitor, siguazodan (10 μM), had little or no effect on IL-2 release or DNA synthesis. This concentration of siguazodan did not enhance the inhibitory action of RP 73401 on IL-2 release but potentiated its effect on DNA synthesis, increasing potency and efficacy. Staph. A-induced DNA synthesis was only partially inhibited by anti-IL-2 neutralizing antibody, whereas dexamethasone (100 nM) and cyclosporine A (100 nM) completely blocked the response. RP 73401 (IC50 6.3 nM) was 140 fold more potent than rolipram (IC50 900 nM) in inhibiting Staph. A-induced [H]-thymidine incorporation into splenocyte DNA. The results implicate a low-affinity form of PDE4 in the suppression of Staph. A-induced IL-2 release from murine splenocytes by PDE inhibitors. The data also indicate that mitogenic factors other than IL-2, whose elaboration or responses to which are regulated by PDE3 as well as PDE4, contribute to the superantigen-induced DNA synthesis.

IT 50847-11-5, Ibudilast
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cAMP phosphodiesterase inhibitors suppress Staphylococcal enterotoxin-A-induced interleukin-2 release from murine splenocytes by interacting with low-affinity phosphodiesterase 4 conformer and not with rolipram binding site)

RN 50847-11-5 CAPLUS

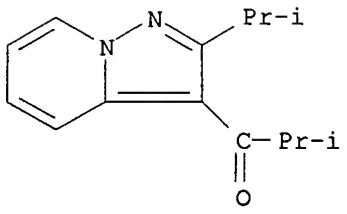
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 40 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:499313 CAPLUS
DOCUMENT NUMBER: 121:99313
TITLE: Effects of ibudilast, an anti-allergic and/or brain vasodilator, on the superoxide generation in human neutrophils
AUTHOR(S): Kobayashi, Masashi
CORPORATE SOURCE: Sch. Med., Gifu Univ., Gifu, 500, Japan
SOURCE: Gifu Daigaku Igakubu Kiyo (1994), 42(2), 161-73
CODEN: GDIKAN; ISSN: 0072-4521
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The effects of ibudilast on the O2- generation in human neutrophils were studied, focused on its site of action. Human neutrophils were prepared by a combination of dextran sedimentation, hypotonic lysis and Ficoll-Paque gradient centrifugation. Development of the O2- production was monitored by measuring chemiluminescence (CL) using a CL enhancer reagent, FCLA with a specific O2- detection. A Ca2+ movement was fluorometrically evaluated using Fura2. All expts. were performed in Hepes supplemented Hanks' balanced salt solution at pH 7.4. After relatively long pre-incubation more than 10 min, ibudilast enhanced O2- generation induced by f-MLP or phorbol myristate acetate (PMA). The drug inhibited the f-MLP-induced CL by pre-incubation up to 10 min, although the PMA-induced CL increased. Thus, ibudilast was characterized as a priming effector, because ibudilast itself did not affect the O2- generation in neutrophils. The priming effect of ibudilast on f-MLP- or PMA-stimulation was amplified by treating the cells with a protein kinase C inhibitor, h-7, whereas the effect on f-MLP-induced CL completely disappeared by treatment with a selective inhibitor of tyrosine kinase, ST-638. Ibudilast increased cyclic-AMP level in f-MLP stimulated cells, suggesting some inhibition of phosphodiesterase. This effect may associate with the effect on Ca2+ movement; inhibition of Ca2+-influx but no effect on release of Ca2+ from vesicles. Ibudilast did not change inositol 1,4,5-triphosphate level and protein kinase C activity in the cells and did not show any effects on phospholipase D dependent CL. These results suggest that ibudilast acts as a priming effector against the stimulated neutrophils via mainly tyrosine kinase. The inhibitory effect on the CL under the relatively short time incubation may be associated with the early and transient increase in c-AMP level. Other mechanisms such as modification of a specific subtypes of protein kinase C response and of functions of cellular factors of NADPH oxidase can be presumed.

IT 50847-11-5, Ibudilast
RL: BIOL (Biological study)
(superoxide formation by human neutrophils priming response to)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)

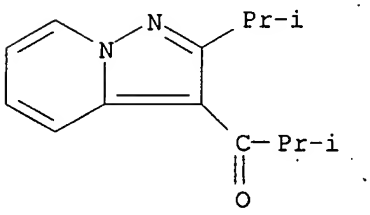


L7 ANSWER 41 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:261003 CAPLUS
DOCUMENT NUMBER: 120:261003
TITLE: Possible role of cyclic AMP phosphodiesterases in the actions of ibudilast on eosinophil thromboxane generation and airways smooth muscle tone
AUTHOR(S): Souness, John E.; Villamil, Maria E.; Scott, Lisa C.; Tomkinson, Adrian; Giembycz, Mark A.; Raeburn, David
CORPORATE SOURCE: Dagenham Res. Cent., Rhone-Poulenc Rorer Cent. Res., Dagenham/Essex, RM10 7XS, UK
SOURCE: British Journal of Pharmacology (1994), 111(4), 1081-8
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English

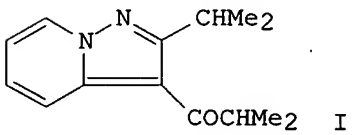
AB The possible role of cAMP phosphodiesterase (PDE) in the inhibitory actions of ibudilast on tracheal smooth muscle contractility and eosinophil thromboxane generation was investigated. Ibudilast was a nonselective inhibitor of partially purified cyclic nucleotide PDE isoenzymes from pig aorta and bovine tracheal smooth muscle, exhibiting only moderate potency against bovine tracheal PDE IV. Similar or slightly lower potencies were displayed against PDEs I, II, III and V. In contrast, rolipram exhibited selectivity for PDE IV. Ibudilast, like rolipram, was a more potent inhibitor of membrane-bound PDE IV from guinea pig eosinophils than of partially purified PDE IV from bovine tracheal smooth muscle. The potency of ibudilast increased when the eosinophil enzyme was solubilized with deoxycholate and NaCl or exposed to vanadate/glutathione complex. In intact eosinophils, ibudilast (0.032-20 μM) potentiated isoprenaline-induced cAMP accumulation in a concentration-dependent manner, being approx. 20-fold less potent than rolipram. Little or no effect on basal cAMP levels was caused by either compound The cAMP-dependent protein kinase activity ratio was increased following incubation of eosinophils with either ibudilast or rolipram in the absence or presence of isoprenaline. Leukotriene B4 (300 nM)-induced thromboxane generation from guinea pig eosinophils was inhibited by ibudilast (IC50 = 11.3 μM) and rolipram (IC50 = 0.280 μM) in a concentration-dependent manner. Ibudilast, while generally less potent than rolipram, produced concentration-dependent relaxation of spasmogen (methacholine, histamine, LTD4)-induced tone in the guinea pig isolated tracheal strip. Ibudilast was less potent in reversing the contractions induced by methacholine than those by histamine or leukotriene D4. Rolipram also exhibited a similar pattern of activity, although the difference in potency against methacholine, compared with that against the other 2 spasmogens, was not as great. These results demonstrate that ibudilast, like rolipram, has several biol. actions on the eosinophil and airways smooth muscle which may be attributed to inhibition of cAMP PDE. These actions may account, at least in part, for the recently reported antiasthma effects of ibudilast.

IT 50847-11-5, Ibudilast
RL: BIOL (Biological study)
(eosinophil thromboxane formation and trachea tone response to, cAMP phosphodiesterase role in)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 42 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:420147 CAPLUS
DOCUMENT NUMBER: 119:20147
TITLE: Inhibition of human platelet aggregation by ibudilast (3-isobutyryl-2-isopropylpyrazolo [1,5-a] pyridine, KC-404)
AUTHOR(S): Murashima, Seiko; Narita, Yugo; Iwasaki, Eiichi; Hashizume, Eiko; Deguchi, Akira; Nishikawa, Masakatu; Deguchi, Katsumi; Shirakawa, Shigeru
CORPORATE SOURCE: Mie Nursing Coll., Tsu, 514, Japan
SOURCE: Nippon Kessen Shiketsu Gakkaishi (1992), 3(6), 392-8
CODEN: NKSGEL; ISSN: 0915-7441
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



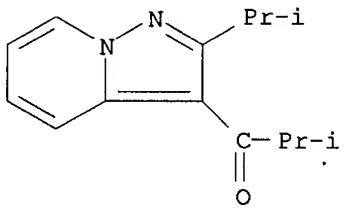
I

AB The effect of a novel compound, 3-isobutyryl-2-isopropylpyrazolo [1,5-a]pyridine (ibudilast, KC-404) (I), on human platelet aggregation and its mechanism of action were investigated. In vitro, KC-404 inhibited human platelet aggregation induced by ADP, collagen, adrenaline, platelet activating factor and arachidonic acid but not by ristocetin. Together, KC-404 and agents which increased cAMP (prostaglandin I2, prostaglandin E1 (PGE1), forskolin) or cGMP (3-morpholinosydnonimine (SIN-1) produced synergistic inhibitory effects on platelet aggregation. KC-404 inhibited human platelet cAMP phosphodiesterase (PDE) (IC50: 50 μM) and cGMP-PDE (IC50: 5.2 μM) activities. CAMP and cGMP concentration of human platelets were not increased by KC-404 itself. PGE1, an adenylate cyclase stimulator, increased cAMP content; KC-404 enhanced the effect of PGE1 on cAMP accumulation. SIN-1, which stimulated guanylate cyclase, increased cGMP content; KC-404 enhanced the effect of SIN-1 on cGMP accumulation. These results suggest that effects of KC-404 on accumulation of cyclic nucleotides and inhibition of platelet aggregation are mediated via inhibition of platelet cyclic nucleotide phosphodiesterase activities.
IT 50847-11-5, KC 404
RL: BIOL (Biological study)

(platelet aggregation inhibition by, of humans, mechanism of)

RN 50847-11-5 CAPLUS

CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 43 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:27556 CAPLUS

DOCUMENT NUMBER: 106:27556

TITLE: A new vasodilator 3-isobutyryl-2-isopropylpyrazolo[1,5-a]pyridine (KC-404) has a dual mechanism of action on platelet aggregation

AUTHOR(S): Ohashi, M.; Okubo, H.; Kito, J.; Nishino, K.

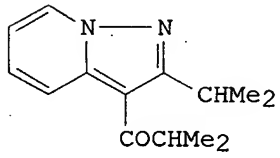
CORPORATE SOURCE: Cent. Res. Lab., Kyorin Pharm. Co., Ltd., Tochigi, 329-01, Japan

SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1986), 283(2), 321-34
CODEN: AIPTAK; ISSN: 0003-9780

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

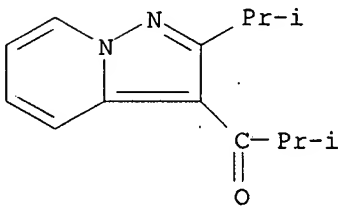


I

AB KC-404 (I) [50847-11-5] at a concentration of ≥4.34 + 10-5 M inhibited ADP-, arachidonic acid- and collagen-induced aggregation of rabbit platelets. In rabbit, KC-404 (0.5 and 2mg/kg, i.v.) caused a decrease in weight of collagen strip extracorporeally superfused with arterial blood, because of a disaggregation of deposited platelet aggregates. This disaggregatory effect of KC-404 was markedly diminished by the pretreatment of animals with aspirin. KC-404 (≥4.34 + 10-6 M) and its major metabolite diOH-KC-404 [101162-42-9] (≥3.78 + 10-7 M) potentiated the anti-aggregatory action of prostacyclin [35121-78-9] on rabbit platelets. KC-404 (≥4.34 +10-8 M) exerted a similar effect in rat platelets. KC-404 had no significant effect on 6-keto-PGF1α and thromboxane A2 formation by rat aortic segment and rabbit platelets, resp. KC-404 inhibited cAMP phosphodiesterase [9036-21-9] (Ki = 91 μM). The present results indicate that KC-404 exhibits its anti-platelet effect via the inhibition of cAMP phosphodiesterase activity in platelets and via the potentiation of anti-aggregatory activity of prostacyclin on platelets.

IT 50847-11-5, KC-404

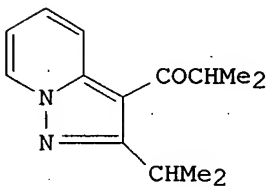
RL: BIOL (Biological study)
(platelet aggregation inhibition by, cAMP phosphodieterase and prostacyclin role in)
RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]- (CA INDEX NAME)



L7 ANSWER 44 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1983:209753 CAPLUS
DOCUMENT NUMBER:	98:209753
TITLE:	Cardiovascular pharmacology of a new vasodilator, 3-isobutyryl-2-isopropylpyrazolo [1,5-a] pyridine (KC-404)
AUTHOR(S):	Irikura, Tsutomu; Kudo, Yoshitaka; Ohkubo, Hideo; Ohashi, Mitsuo; Kito, Junshi; Nishino, Keigo
CORPORATE SOURCE:	Cent. Res. Lab., Kyorin Pharm. Co., Ltd., Tochigi, 329-01, Japan
SOURCE:	Oyo Yakuri (1983), 25(2), 283-90 CODEN: OYYAA2; ISSN: 0369-8033
DOCUMENT TYPE:	Journal
LANGUAGE:	Japanese

GI



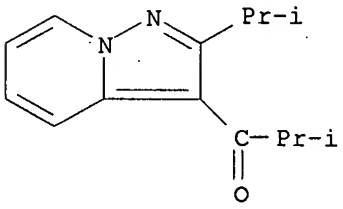
I

AB The cardiovascular pharmacol. of KC-404 (I) [50847-11-5] a new vasodilator, was studied in anesthetized dogs and in isolated guinea-pig heart and atria. The effect of I on cyclic 3', 5'-AMP phosphodiesterase [9036-21-9] was also investigated. In anesthetized dogs, I (0.1 and 0.5 mg/kg, i.v.) produced an increase in blood flow of several vascular beds in a dose-dependent manner. The order of potency to produce vasodilation was: vertebral, femoral > coronary > internal carotid, mesenteric > renal arteries. The vasodilator actions of I on vertebral, internal carotid, and coronary arteries were 6.0, 5.4, and 1.6 times, resp., as potent as papaverine. The decrease in systemic blood pressure caused by I was transient and less marked than that of papaverine. I.v. I at a low dose (0.01 mg/kg) produced a significant increase in vertebral arterial blood flow without affecting femoral arterial. In anesthetized open-chest dogs, I produced a slight increase in heart rate, cardiac output, and cardiac work with a significant decrease in total peripheral resistance. Moderate increases in heart rate

and coronary blood flow, which were not affected by propranolol, were also observed in isolated guinea-pig heart after injection of 30 μg I. In isolated guinea-pig atria, a dose-dependent increase in heart rate was caused by I at concentration 10-8 g/mL, the maximum response attained at 10-5 g/mL was about one third that of isoproterenol. Propranolol had no influence on the increase in heart rate caused by I or papaverine. I competitively inhibited cyclic AMP phosphodiesterase one from various tissues, notably from canine basilar and femoral arteries and guinea-pig trachea. I was somewhat less active in this regard compared with papaverine. Thus I produced a dose-dependent increase in blood flow of several vascular beds with selectivity for cerebral circulation as compared with papaverine. In addition, the vasodilator effect of I may partly be mediated through inhibition of cyclic AMP phosphodiesterase.

IT 50847-11-5
RL: BIOL (Biological study)
(cardiovascular pharmacol. of)

RN 50847-11-5 CAPLUS
CN 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]-
(CA INDEX NAME)

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L2               7 S L1
L3             103 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 12:27:45 ON 20 JUL 2007
L4             222 S L3 FULL
L5             158 S L4 AND PY<2002
L6              44 S L4 AND PHOSPHODIESTERAS?
L7              44 S L6 AND INHIBIT?

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                                                   ENTRY    SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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